"PROSPECTIVE RANDOMISED CONTROL STUDY FOR COMPARING THE EFFICACY OF EPIDURAL DEXMEDETOMIDINE AND BUPRENORPHINE WITH 0.5% BUPIVACAINE IN LOWER LIMB ORTHOPAEDIC SURGERIES"

Dissertation submitted to

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in partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

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BRANCH X

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MADRAS MEDICAL COLLEGE

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APRIL 2013

CERTIFICATE

This is to certify that the dissertation entitled, **"PROSPECTIVE RANDOMISED CONTROL STUDY FOR COMPARING THE EFFICACY OF EPIDURAL DEXMEDETOMIDINE AND BUPRENORPHINE WITH 0.5% BUPIVACAINE IN LOWER LIMB ORTHOPAEDIC SURGERIES"** submitted by **Dr.S.VIJAYANANDH**, in partial fulfilment for the Degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr. M.G.R. Medical University, Chennai., is a bonafide record of the work done by him in the INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE, Madras Medical College and Rajiv Gandhi Government General hospital, during the academic year 2010-2013.

Prof Dr.M.VASANTHI, M.D.,D.A, DNB
DIRECTOR AND PROFESSOR,
Institute Of Anaesthesiology
And Critical Care,
Madras Medical College,
Chennai - 600 003.

Dr. V. KANAGASABAI, M.D.
DEAN,
Rajiv Gandhi Government,
General Hospital,
Chennai - 600 003.

DECLARATION

I, **Dr.S.VIJAY ANANDH**, solemnly declare that this dissertation entitled **"PROSPECTIVE RANDOMISED CONTROL STUDY FOR COMPARING THE EFFICACY OF EPIDURAL DEXMEDETOMIDINE AND BUPRENORPHINE WITH 0.5% BUPIVACAINE IN LOWER LIMB ORTHOPAEDIC SURGERIES"** is a bonafide work done by me in the Institute of Anaesthesiology and Critical Care, Madras Medical College and Rajiv Gandhi Government General hospital, Chennai, during the period 2010 to 2013 under the guidance of **Prof. Dr. M.VASANTHI, M.D., D.A.**, **DNB,** Director, Institute of Anaesthesiology and Critical Care, Madras Medical College and Government General Hospital, Chennai – 3 and submitted to **The TamilnaduDr. MGR Medical University,** Guindy, Chennai – 32, in the partial fulfillment of the requirements for the award of the degree of MD Anaesthesiology (Branch X).

Place: Chennai,
Date:

(Dr.S.VIJAY ANANDH)

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CONTENTS

INTRODUCTION

Injection of local anaestheic into the epidural space to produce reversible loss of all modalities of sensations as well as motor functions is termed as epidural anaesthesia. Although techniques of epidural anaesthesia do not offer the economy of drug dosage or degrees of blockade of spinal anaesthesia, they have an added advantage of continuing post operative analgesia through the catheter in the epidural space.

Epidural anaesthesia is more versatile and is being used extensively in fields of surgical anaesthesia, obstretic analgesia , management of acute or chronic pain

Since 1940's when epidural neuraxial blockade was first described studies have been extensively conducted to identify an ideal adjuvant for epidural anaesthesia along with the local anaesthetic . As epidural neuraxial blockade requires large volume local anaesthetic attempts are being made to identify an adjuvant which would decrease the requirement of local anaesthetic, fasten the onset of action of local anaesthetic, produce sedation,maintain hemodynamic stability and prolong the duration of sensory blockade.

Opioids are being traditionally used as adjuvants in epidural neuraxial blockade as they produce sedation and have inherent analgesic activity. Recently α2 agonist like dexmedetomidine and clonidine are being studied as they have most of the desirable qualities of an ideal adjuvant.

Buprenorphine is a long acting agonist anatagonist opioid with high affinity to μ receptors and 33 times more potent than morphine[2] can be used as an adjuvant in epidural anaesthesia.

Dexmedetomidine, a highly selectively α_{2A} agonist which produces both sedation and augments the analgesic action of local anaesthetic[2]when it is given epidurally.

Keeping in mind the pharmacological interactions and adverse effects of Buprenorphine and Dexmedetomidine, we planned to conduct a double blinded prospective randomized control study in patients undergoing lower limb orthopaedic surgeries under epidural anaesthesia. We used 0.5% bupivacaine and either one of the above two drugs epidurally with an aim of comparing the perioperative analgesic efficacy, sedation and hemodynamic stability of these 2 drugs given epidurally

EPIDURAL ANAESTHESIA

ANATOMY OF EPIDURAL SPACE :

The epidural space is a saw tooth shaped space extending from the base of skull to Sacro-Coccygeal membrane and has direct communications with paravertebral space and indirect communications with the CSF. Epidural space is not as voluminous as subarachanoid space.

BOUNDARIES OF EPIDURAL SPACE[1]:

Superiorly	-	Foramen magnum.
Inferiorly	-	Sacral hiatus and sacrococcygeal membrane.
Laterally	-	Periosteum of pedicles of vertebrae and inter vertebral foramen.
Anteriorly	-	Posterior longitudinal ligament covering vertebral bodies and intervertebral discs.
Posterior	-	Periosteum of anterior surfaces of lamina.articular process and connecting ligaments and interlaminar spaces filled by the ligamentum flavum.

CONTENTS OF EPIDURAL SPACE:

It is a potential space filled with epidural pad of fat, areolar tissues, lymphatics, epidural plexus of veins (Batson's plexus), nerve roots that traverse it . Of prime importance are the epidural pad of fat and venous plexus. It is postulated that volume of fat in the epidural space explain the age related changes in epidural dose requirement. Obese individuals have more fat, as age increases the volume of fat decreases .

Large valveless epidural veins are part of internal vertebral venous plexus. These plexus have rich segmental connections at all levels. Within intervertebral foramina and epidural space by the way of intervertebral foramina epidural venous plexus communicate with thoracic and abdominal veins. So any pressure change in these cavities are transmitted to the epidural veins. Therefore in conditions like, pregnancy, vena caval obstructions, caution must be taken during epidural neuraxial blockade .

Important aspects that should be taken care are[1]

1. Epidural needle insertion must be in midline to avoid large laterally placed epidural veins.

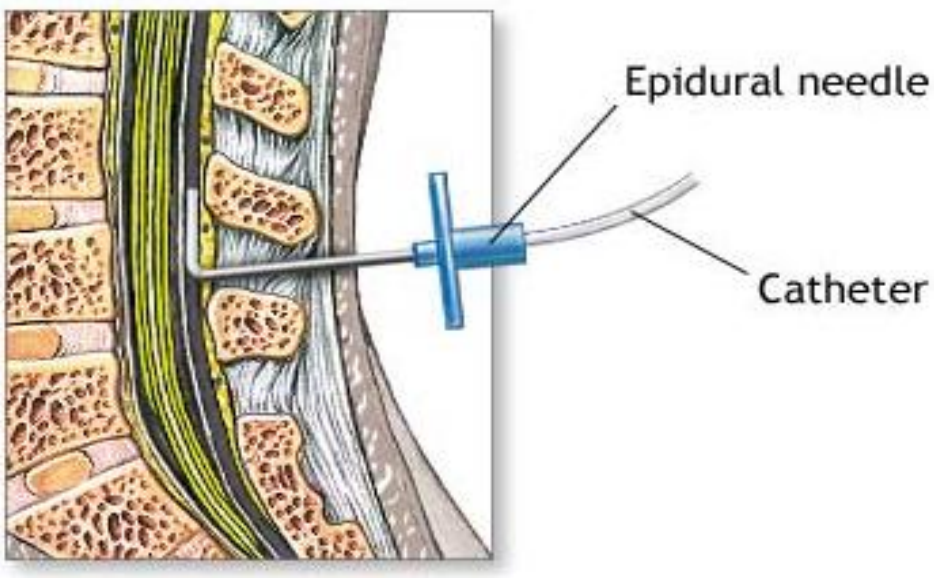
2. Insertion of epidural needle or catheter should not be done during episodes of marked increase in size of epidural veins such as with increased thoraco-abdominal pressure during straining in case of labor analgesia.

3. Presence of vena caval obstruction calls for a reduction in dose, decreased rate of injection and increased care during aspiration.

A unique feature of epidural veins that is of importance is, draining of CSF and transfer of local anaesthetic to CSF through regions of dural cuffs where the subarchanoid space invaginates the epidural veins.

STRUCTURES PIERCED DURING EPIDURAL NEEDLE INSERTION[1] :

- Skin
- Subcutaneous tissue.
- Suprapinous ligament.
- Interspinous ligament.
- Ligamentumflavum.
- Epidural space.



PHYSIOLOGY OF EPIDURAL NEURAXIAL BLOCKADE :

The site of action of local anaesthetic is the spinal nerve roots. Lumbar segmental nerve roots are mixed nerves that contain, autonomic, somato sensory and motor nerve fibres.

- Pre ganglionic Sympathetic efferent blockade of (T_1 - L_2) segments leads to peripheral vasodilation.

- Sensory blockade - afferent blockade of both somatic and visceral pain stimuli.

- Motor blockade - efferent blockade leading to varying degrees of motor paralysis and reflex muscle relaxation without paralysis due to ‘deafferentation.’

Injection site of epidural anaesthetic must be close to the desired nerve roots to be blocked to reduce the volume of local anaesthetic required and to reduce complications of systemic absorption.

Differential neural blockade which is a feature of subarachanoid blockade is also seen in epidural blockade , this means different types of nerve fibres differ in their sensitivity to the local anaesthetic.

Pre ganglionic Sympathetic fibres are usually blocked first followed by pain/temperature, followed by motor blockade.

Autonomic block is of one or two segments higher than sensory blockade which is one or two segments higher than that of motor blockade.

Physiologic effects of epidural blockade depend upon the spinal level and number of segment to be blocked. High thoracic and extensive epidural blocks produce profound sympathetic blockade. Usually, lumbar epidural blockade does not produce extensive neuraxial blockade and profound physlogic effect on the cardiovascular system.

PHARMACOLOGY OF EPIDURAL BLOCKADE:

For a successful epidural blockade, the anaesthesiologist should understand the physiology of nerve conduction and pharmacology of local anaesthetics.

The number of segments to be blocked should be calculated and the tip of the epidural catheter should be placed in such a way that it could cover all the required segments with optimal volume of drug.

Potency, duration of action of the drug and its ability to preferentially block different types of nerve fibers should also be taken into consideration.

MECHANISM OF ACTION OF LOCAL ANESTHETIC:

Local anaesthetics bind to the sodium channel in the nerve fibres in the active state and blocks the activation of sodium channel. Thus preventing the movement of sodium ions. This blocks the generation of Action potential known as membrane stabilization effect (i.e.) further nerve stimulation will not affect the resting membrane potential.

SPECIFIC TO EPIDURAL SPACE:

- Sensory block due to blockade of Na^+ channels in dorsal horn and motor block due to blockade of Na^+& K^+ ion channels in ventral horn.

- In addition they also block release of substance P which is involved in pain signal processing.

- Blockade of the voltage gated Ca++ channel pre synaptic level is responsible for indirect action of centrally administered local anaesthetics which blocks the release of neurotransmitters like glutamate substance P, calcitonin gene related peptide, neurokinin 1,2 (NK1, NK2)

FACTORS AFFECTING EPIDURAL BLOCKADE :

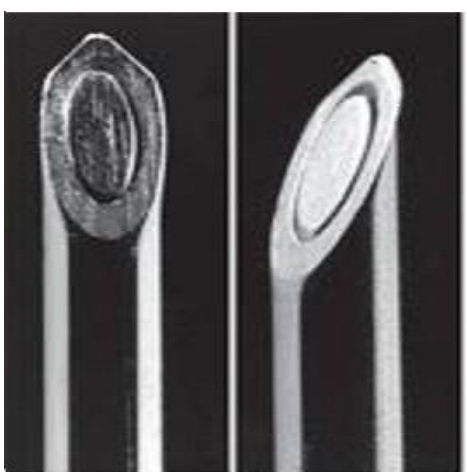
1. Site of injection.
2. Size of Nerve root.
3. Posture- sitting -minimally lateral - definitely
4. Drug used(long acting /short acting)
5. Dose (volume / concentration)
6. Addition of epinephrine.

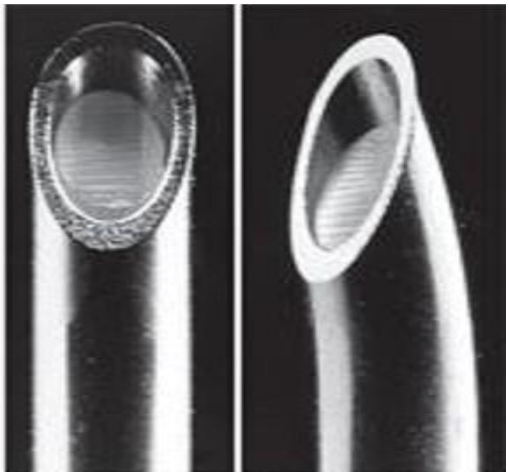
7. Number & frequency of injection.

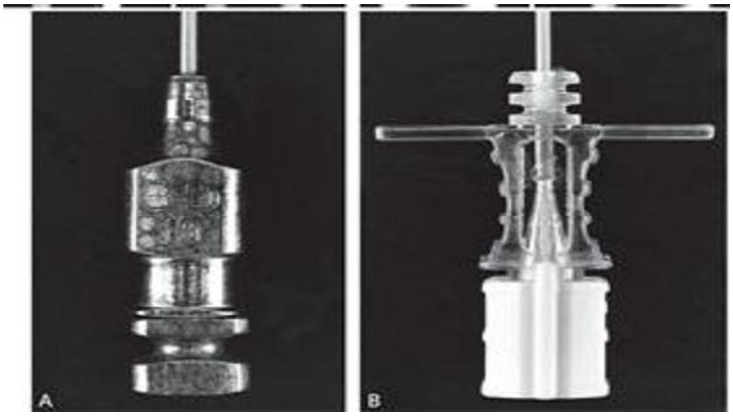
8. Speed of injection

EPIDURAL EQUIPMENTS[3]:

Epidural needles : Tuohy's , Crawford needle .







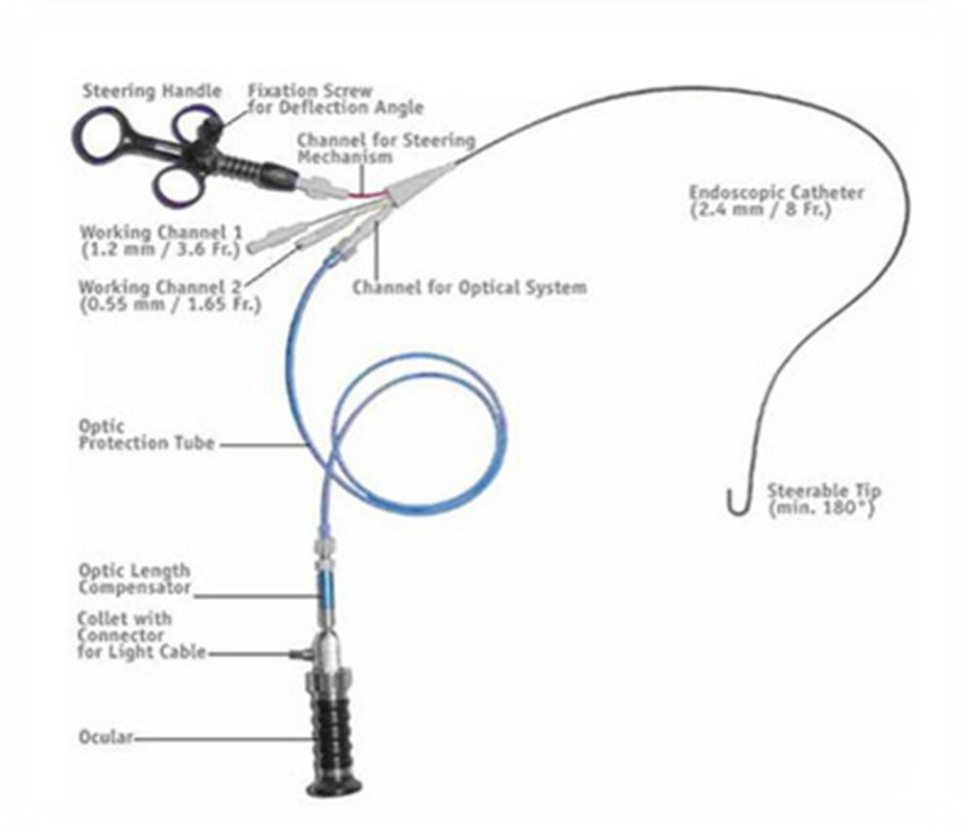
Epidural catheters:

Open tip closed, closed tip with single lateral port, closed tip with 3 radially arranged ports.

RECENT ADVANCE :

Ultrasonography and Epiduroscope have been recently introduced in the armamentarium to identify epidural space.

Epiduroscope plays a major role in percutaneous epidural neurolysis in chronic pain management.

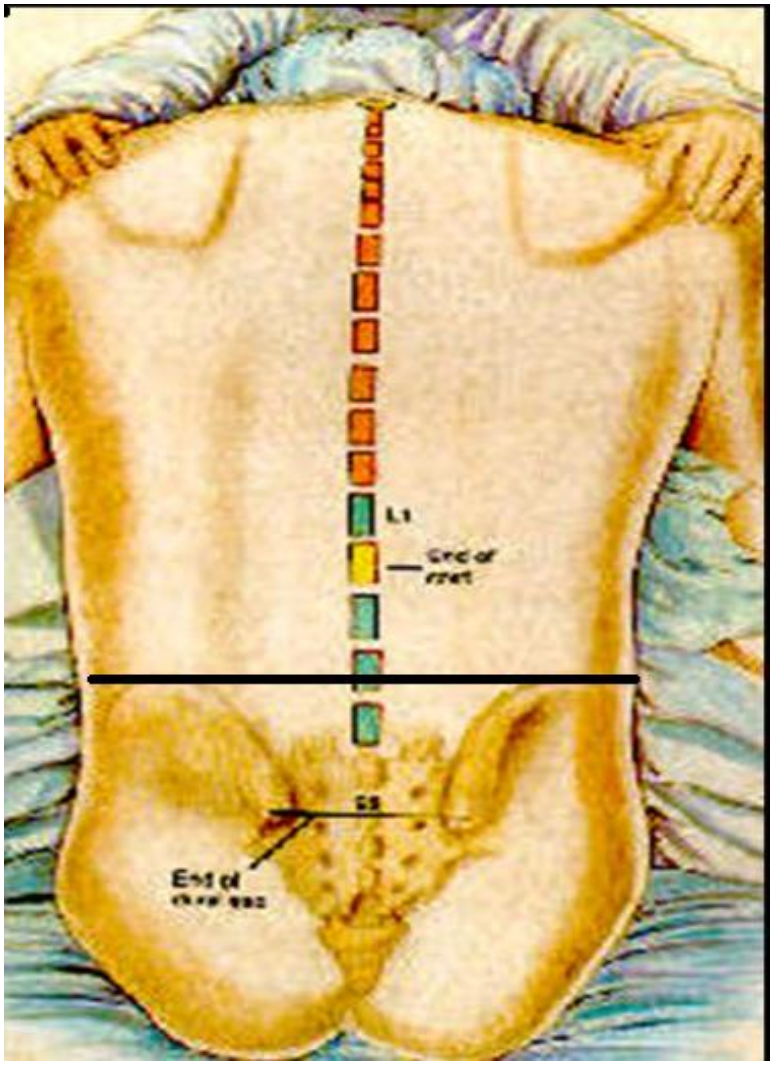


TECHNIQUE

1. Midline approach

2. Paraspinous approach

Positioning :



INDICATIONS:

1) Surgery

   a. Upper & lower abdominal surgery for intra and postoperative pain management

   b. Urological surgeries

   c. Thoracic surgeries.

2) Postoperative and post trauma pain relief.

3) Obstetric anesthesia and analgesia.

4) Diagnosis and management of chronic pain.

5) Epidural steroids and narcotics

6) Newer techniques - Epidural electrical stimulation.

CONTRA INDICATIONS:

***Absolute*:**

- Patient refusal.
- Major coagulation disorders.
- Uncorrected hypovolemia.
- Infection at site of injection.
- Severe sepsis.

Relative:

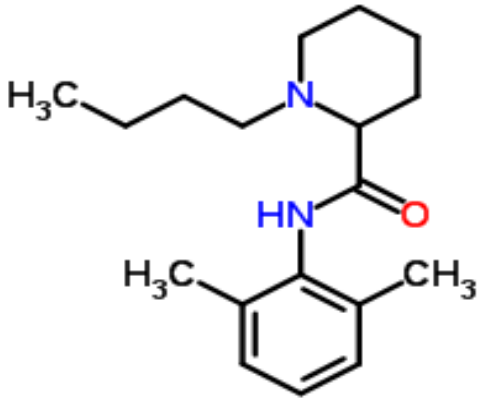
- Pre-existing neurological deficit.
- Spine deformities.

COMPLICATIONS:

1. Director trauma to nerve and nerve roots.
2. Epidural hematoma
3. Abscess
4. Neurotoxicity
5. Anterior spinal artery spasm due to needle injury or by use of epinephrine.
6. Missed segments - patching uptake of blockade.
7. Inadequate motor block
8. Sacral sparing.
9. Inadvertent dural puncture
10. Subdural communication
11. Cannulation into an epidural vein.

PHARMACOLOGY OF BUPIVACAINE

STRUCTURE[2] :



CHEMICAL COMPOSITION :

Bupivacaine Hydrochlorideis an amide group of local anaesthetic2-Piperidinecarboxamide, 1-butyl-N-(2,6-dimethylphenyl)-mono-hydrochloride and is formed by addition of a butyl group to the piperidine nitrogen of Mepivacaine making it 35 times more potent. Local anesthetics prevent transmission of nerve impulses (conduction blockade) by inhibiting the passage of sodium ions through selective sodium channels in nerve membranes. However, they do not alter the resting membrane potential or threshold potential.

MECHANISM OF ACTION :

Bupivacaine binds to alpha subunit of the sodium channel

⇩

Sodium channels exist in activated-open,

inactivated-closed and resting-closed.

⇩

Bupivacaine selectively binds to sodium channels in

inactivated-closed

⇩

Prevent their change to rested-closed, activated-open states.

⇩

Sodium channels are not permeable in inactivated-closed state

⇩

No conduction of impulses and No action potential occurs

Frequency dependent blockade :

Sodium ion channels tend to recover from local anesthetics induced conduction blockade between action potentials and to develop additional conductional blockade. Local anesthetics gain access to receptors only when sodium channels are in activated-open states. So, a resting nerve is less sensitive to conduction blockade than a repetitively stimulated nerve.

Other Sites Of Action :

In addition to sodium channels bupivacaine blocks voltage dependent potassium ion channels. This explains the reason for broadening of action potential. Bupivacaine also blocks the calcium ion channels (L-type). Bupivacaine blocks both types of pain fibres, myelinated A-delta and unmyelinated C-fibres. Preganglionic-B fibres are readily blocked by local anesthetics than the other two nerve fibres.

PHARMACOKINETICS:

Bupivacaine is a weak base that has a pKa value above the physiological pH. Hence only less amount of the drug is in non-ionised form. Acidosis increases the pH of the medium increasing the ionised

fraction of the drug resulting in poor quality of anaesthesia. Absorption of the drug depends on site of injection, its dosage, adjuvants such as epinephrine, opioids, and the pharmacological characteristics of the drug. The plasma concentration is determined by the rate of tissue distribution and rate of clearance. The lungs are capable of extraction of bupivacaine from the systemic circulation and its first pass pulmonary extraction is dose dependent. Bupivacaine binds to the plasma protein alpha-1 acid glycoprotein.

Metabolism :

Bupivacaine Hydrochloride is metabolised primarily in the liver. It undergoes aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation with glucuronic acid. Patients with hepatic disease may be more susceptible to the toxicities of the amide-type local anesthetics. Pipecoloxylidine is the major metabolite of Bupivacaine Hydrochloride. Only 6% of Bupivacaine is excreted unchanged in the urine.

Onset	**Slow**
Duration of action	240-480 mins
pK	8.1
Protein binding	95%
Lipid solubility	1
Volume of distribution	73 litres
Clearance	0.47 litres/min
Elimination half time	210 mins

USES:

Regional Anaesthesia – (i) Local infiltration (ii) Peripheral nerve block (iii) Epidural anesthesia(iv) Spinal anesthesia (v) topical anaesthesia.

Concentration Used	**Maximum Permitted Dose**
0.125%-0.5% (preservative)	3mg/ kg body weight
0.75% (not to be used in obstretic epidurals)	Max. over 4 hrs-150mg Max. During 24 hrs-400 mg
0.5% plain/hyperbaric solution (intrathecal use)	20 mg

SIDE EFFECTS:

a. Allergic reactions

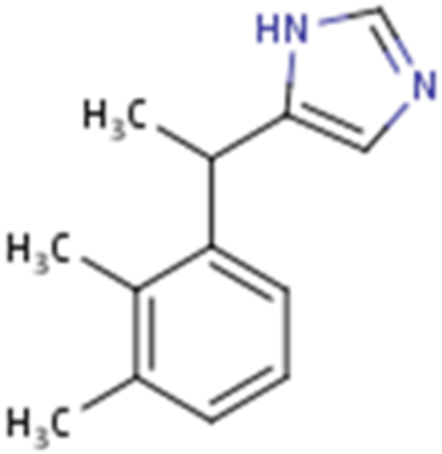
b. Neurotoxicity – tinnitus , vertigo , muscle twitches , slurred speech and seizures.

c. Cardiotoxicity – precipitous hypotension, cardiac dysrhythmias and atrioventricular blocks.

d. Hepatotoxicity

PHARMACOLOGY OF DEXMEDETOMIDINE

STRUCTURE [2]:



CHEMICAL COMPOSITION :

Imidazole derivative, Active s-Enantiomer of Meditomidine (+)-4-(S)-[1-(2, 3-dimethylphenyl) ethyl]- 1H-imidazole monohydrochloride. It is a highly selective α2a agonist (α2 :α1 = 1600:1)

MECHANISM OF ACTION :

Specific alpha 2 adrenoceptoragonist, acts through post synaptic α2 receptors by increasing conductance through potassium channels

PHARMACOKINETICS :

95% protein bound with a volume of distribution 1.5 L/kg.with at1/2α (rapid distribution) of 6 minutes and t1/2β (elimination half life) of 2-3 hours.

METABOLISM :

By Conjugation (41%) and N-methylation(21%).Inactive metabolites excreted in urine and faeces.

PHARMACODYNAMICS :

Central nervous system :

Unique sedative property, patients will be sedated but arousable without respiratory depression .

Cardiovascular system :

Reduces HR and SVR. There is a biphasic response on blood pressure.

Respiratory system :

Reduces minute ventilation, retains response to hypercarbia

ROUTES OF ADMINISTRATION :

Intravenous, Intramuscular, Epidural, Intrathecal, Intranasal

DOSE :

Loading dose : 0.5-1.0µg/kg over 10 minutes.

Maintenance dose : 0.3-0.7µg/kg/hr not exceeding 24 hours

CONTRAINDICATIONS :

Known hypersensitivity to the drug

USES :

1. **ICU sedation** in mechanically ventilated patients

2. **In anaesthesia**

   a. before induction-at a dose of 0.3-0.67µg/kg given before 10-15 minutes attenuates the hemodynamic response to intubation

   b. as a premedication 2.5µg/kg

   c. sedation during regional anaesthesia

   d. as an adjuvant in bariatric surgery, craniotomy aneurysm, sleep apnea patient.

3. **Procedural sedation :**

   a. for securing the airway during awake fibreoptic intubation.

   b. for bronchoscopy

ADVERSE EFFECTS :

Most common are

   a. Hypotension

   b. Bradycardia

   c. Dry Mouth

   d. Hypertension

   e. Arrythmias

   f. AV block

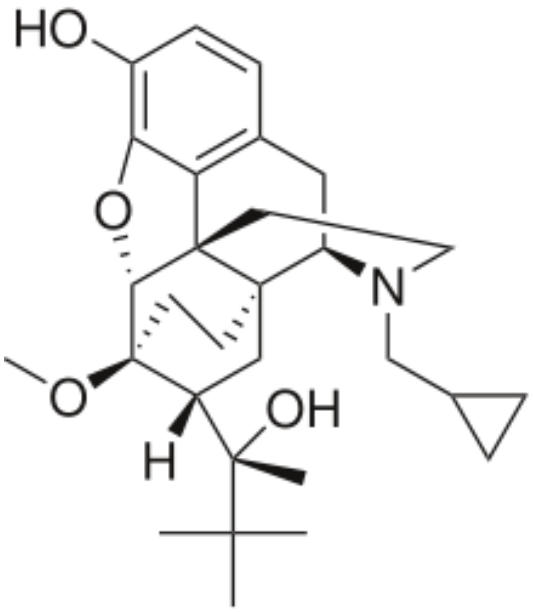
ALPHA 2 ANTAGONIST :

Atipamezole:

Scheinin *et al.* reported about the ability of atipamezole, a novel selective α2-adrenoceptor antagonist, to reverse the sedative properties of intramuscular dexmedetomidine were dose-dependently antagonized by intravenous atipamezole. However, the sensitivity for reversal of these two responses may be different.Because the agonist and the antagonist have similar elimination half-lives, the likelihood of recurrence of the clinical effects of dexmedetomidine after reversal byatipamezole is small. Therefore the alpha 2 agonists providea titratable form of hypnotic sedation that can be reversed readily.

PHARMACOLOGY OF BUPRENORPHINE

STRUCTURE[2] :



CHEMICAL COMPOSITION :

Synthetic derivative of thebaine

MECHANISM OF ACTION :

Partial agonist at μ receptor and dissociates very slowly leading to prolonged duration of analgesia,also has high affinity to kappa receptor but less intrinsic activity .

DOSE:

Intravenous, Intramuscular	0.3 – 0.6 mg, 8^{th} hourly
Sublingual	0.2 -0.4 mg, 8^{th} hourly
Epidural	upto 0.3 mg
Intrathecal	0.15 mg

PHARMACOKINETICS :

Drug undergoes significant first pass metabolism when given orally so sublingual route is preferred, bioavailability is 40-90% when given intramuscular.Volume of distribution is 3.2 L/kg, 90% protein bound

Metabolism :

Undergoes hepatic metabolism by dealkylation and conjugation to glucuronides which are lipid soluble and excreted in bile. Elimination half life is 5 hours

PHARMACODYNAMICS :

Cardiovascular system :

Minimal effects on CVS reduces heart rate by less than 25%, systolic blood pressure may fall by 10%

Central nervous system :

Nearly 33 times more potent than morphine. Produces meiosis and analgesia as like other opioids, reduces cerebral glucose metabolism, reduces gastric motility and has emetic effect.

Respiratory system :

Produces respiratory depression and increases the threshold for hypercapneic ventilator drive. Has a ceiling effect.

ADVERSE EFFECTS:

- ✓ Drowsiness
- ✓ Confusion
- ✓ Nausea, vomiting
- ✓ Headache
- ✓ Pruritis
- ✓ Urinary retention.

OPIOID ANTAGONIST :

- **Naloxone**
- **Naltrexone**
- **Nalmefene**

They are pure μ receptor antagonist with no agonist activity.

Naloxone,the most commonly used opioid antagonist could not be used to reverse all the effects of Buprenorphine as it is a partial agonist.

Naloxone, at a dose of 1-4μg/kg i.v usually reverses opioid induced analgesia and respiratory depression but due to its shorter duration of action a continuous infusion at the rate 5 μg/kg/hr is recommended.

REVIEW OF LITERATURE

Sukhminder Jitsingh Bajua et al.,[4](2011) studied the efficacy of epidural dexmedetomidine and fentanyl when combined with ropivacaine. 100 patients of age group 21-56 years and ASA physical status I & II who underwent lower limb orthopaedic surgeries were randomly allocated in 2 groups RD and RF groups

RD - Ropivacaine (15ml of 0.75%) + Dexmedetomidine(1 µg/kg)

RF-Ropivacaine(15ml of 0.75%) + Fentanyl (1 µg/kg)

Routine cardio-pulmonary monitoring parameters like NIBP, $SPO_{2,}$ECG were recorded. Both groups were compared based on various block characteristics time to onset of analgesia at T10, maximum sensory analgesic level, time to max sensory blockade, time to two segmental regression and sedation scores.

Demographic profile of patients were comparable. Onset of analgesia, complete motor blockade and duration of post operative of analgesic were prolonged significantly in RD groups. Sedation scores were better with RD. Incidence of nausea and vomiting was significantly higher in RF group.

Consumption of local anesthetic for post operative analgesia was significantly low and RD group. To conclude demexdetomidine is a better adjuvant for epidural neuraxial blockade than fentanyl at a dose of 1 µg/kg.

Sukwinder Kaur Bajua et al.,[5] (2011) did a comparative evaluation of epidural dexmedetomidine and clonidine in patients undergoing vaginal hysterectomies.50 patients undergoing vaginal hsytrectomies were randomly allocated in 2 groups : RD andRC.

RD - Ropivacaine (17 ml of 0.75%) + Dexmedetomidine(1.5 µg/kg)

RC- Ropivacaine (17 ml of 0.75%) + Clonidine (2 µg/kg)

Onset of analgesia, sensory and motor blockade, sedation level, duration of analgesia and adverse effects were compared. Demographic profile, initial and postoperative block variables and cardio pulmonary parameters were comparable not significant in both groups. Whereas sedation was better in RD group and incidence of side effects was less in RD group.

Sandip Sinha et al.,[6] (2012) did a comparative study of analgesic efficacy of plain Ropivacaine vs Ropivacaine with Dexmedetomidine in Paravertebral block for unilateral renal study.

60 patients of ASA I & II undergoing unilateral renal surgery were allocated into 2 groups Group I - only Ropivacaine, Group II - Ropivacaine + Dexmedetomidine (1 µg/kg)

After administration of GA, parevertebral catheter was placed and block given with only. 0.25% Ropivacaine 18ml in group I and 0.25% Ropivacaine18ml + Dexmedetomidine 1µg/kg in group II. Postoperative pain relief was compared after extubation by using VAS scale.

Mean duration of analgesia was longer in Group II & total consumption of Ropivacaine was less in Group II. Addition of Dexmedetomidine to Ropivacaine significantly prolongs duration of Analgesia in Paravertebral block.

Kiran agarwal et al.,[7](2010) compared the analgesic efficacy of buprenorphine vs clonidine with bupivacaine in lower segment caesarean section.

112 female patients undergoing LSCS were allocated to 3 groups.

a) 0.125%Bupivacaine + Buprenorphine (0.075mg)

b) 0.125% Bupivacaine + Clonidine (37.5mg)

c) 0.125% Bupivacaine plain were administered epidurally.

and quality of postoperative pain relief was compared using VAS scale.

Mean duration of analgesia was significantly more in Buprenorphine group.

There was no respiratory depression in all 3 groups, Hypotension, Sedation were comparable in both Group I, II and less in group III.

Epidural buprenorphine produces prolonged postoperative analgesia and is safe in LSCS patients.

Egon Lanz et al.,[8](1984) did a double blind study comparing different doses of Epidural Buprenorphine 158 patients were allocated into 3 groups and were given either 0.15 mg epidural. Buprenorphine, 0.3 mg in 15ml saline after 2% Mepivecaineanaesthesia, 0.3 mg Buprenorphine after 0.5% Bupivacaine and control group.

The need for additional analgesics as well as side effect were observed. Analgesia after 150mg of Buprenorphine was superior to no reinjection (control group) after 6 hrs of surgery. 300mg of Buprenorphine was superior to both groups until twelfth hour. There was increase in $PaCO_2$ 2-5 mm of Hg between 2-4 hrs after

administration 0.3 mg of Buprenorphine. There was no evidence of respiratory depression. Other side effects were comparable in all groups.

They concluded 300 micrograms of Epidural Buprenorphine could be given safely for postoperative analgesia following lower limb orthopaedicsurgeries.

Sara Korula et al.,[9](2010)compared epidural and intrathecal Buprenorphine using combined spinal epidural technique for caesarean section.

90 patients undergoing LSCS (elective) of ASA I physical status were allocated into 3 groups to evaluate the analgesic effect of neurexial buprenorphine.

Group I - 150 µg	Buprenorphine intrathecally.
Group II - 150 µg	Buprenorphine epidurally.
Group III - 300 µg	Buprenorphine epidurally.

They observed the following results.

Group I and Group III had much longer duration of Analgesia than group II.

Group III had similar postoperative duration of analgesia as Group I without compromising patient safety and neonatal outcome with less side effect than Group I. Thus, they concluded that 300µg of Buprenorphine epidurally is equianalgesic to 150µg of intrathecally.

Vijay G. Anand et al.,[10](2011) compared the effects of caudal Dexmedetomidine combined with Ropivacaine in children undergoing lower abdominal surgeries.

60 children were allocated into 2 groups.

Group RD - 2 µg/kg Dexmedetomidine + 1ml/kg of 0.25% Ropivacaine.

Group R- 1 ml/kg of 0.25% Ropivacaine.

Inhalational induction was done with O_2: N_2O , 1:1 and 8% Sevoflurane. After LMA insertion caudal block was given with the study drugs. Duration of postoperative analgesia was noted. It was significantly high in RD group.

Intraoperative and postoperative hemodynamics were stable in both groups. They concluded that caudal Dexmedetomidine2 µg/kg with 0.25%Ropivacaine 1ml/kg for lower abdominal surgeries resulted in better quality of analgesia, induced sleep and less side effects.

Rajni Gupta et al.,[11](2011) compared intrathecal Dexmedetomidine and fentanyl as adjuvants to Bupivacaine in 60 patients undergoing lower abdominal surgeries, they were allocated into 2 groups and received either 12.5mg hyperbaric bupivacaine + 5µgdexmedetomidine (group D) . 12.5 mg Hyperbaricbupivacaine + 25µg of fentanyl (group F) . They observed that patient in group D had longer sensory and motor blockade and reduced demand for rescue analgesia for 24 hours.

Tanmoy et al., [12](2010) studied the effect of adding Magnesium sulphate or Clonidine in epidural route along with Bupivacrine 0.5% in patients coming for lower abdominal and lower limb procedures.

Group B -19 ml of 0.5%Bupivacaine + 1ml $MgSO_4$ (50mg)

Group C - 19 ml of 0.5% Bupivacaine + 1ml of Clonidine (150mg)

Group A - 19 ml of 0.5% Bupivacaine + 1ml of Normal saline

These groups were compared under the following criterias:

- ✓ Time of onset of sensory block to T6 level.
- ✓ Time to 2 segment regression.
- ✓ Time for first epidural top up .
- ✓ Sedation etc.

They concluded that administration of epidural $MgSO_4$ with bupivacaine produced predictable early onset of anaesthesia without any side effects and addition of clonidine prolongs analgesia and sedation.

AIM OF THE STUDY

To compare the perioperative analgesic efficacy and haemo dynamicstability of epidural Buprenorphine and Dexmedetomidine with 0.5% Bupivacaine in lower limb orthopaedic surgeries.

MATERIALS AND METHODS

STUDY DESIGN: Prospective, randomised, double blinded (subject/observer) study.

STUDY SIZE: 80 Patients**.**

RANDOMISATION : By closed envelope method.

INCLUSION CRITERIA :

- Age : 16 years to 60 years.
- ASA : I & II.
- Surgery : Elective lower limb surgeries.
- Only those who have given valid informed consent.
- Weight : 50 kg to 80 kg.

EXCLUSION CRITERIA :

- Not satisfying inclusion criteria.
- Patients with short stature less than 145 cm and spine abnormalities.
- Pregnant females.
- Any contraindication to epidural anaesthesia like abnormal coagulation profile.

MATERIALS REQUIRED:

- 17 G Tuohy's Epidural needle and 19 G catheter.
- Drugs – 0.5% Bupivacaine for epidural anaesthesia, inj. Buprenorphine, inj. Dexmedetomidine, distilled water, inj. Ephedrine, inj. Atropine and other emergency drugs and 2% Lignocaine for local anaesthesia of the skin.
- Monitors – ECG , NIBP , SPO2 .
- 2 cc syringe and 5 cc syringe.
- Betadine, spirit, gauze to disinfect the back.
- 16G,18G intravenous cannula.
- 0.9% Normal saline and Ringer lactate.

PRE-OPERATIVE ASSESSMENT:

In all patients, age, body weight and baseline vital parameters were recorded. History regarding previous anaesthesia, surgery and significant comorbid illness, medications and allergy was recorded. Complete physical examination and airway assessment were done.

In the preoperative period all patients were instructed about the benefits of epidural analgesia and also informed consent was obtained from all the study group patients.

PREMEDICATION:

All patients were premedicated with T.Alprazolam 0.25-0.5mg, at 6 am on the day of surgery. inj. Ranitidine 50 mg i.v and inj. Emeset 8mg i.v was given 30 minutes before surgery .

MONITORS :

Standard monitors like ECG, Non-invasive BP, and spO2 were connected to the patient.

I VACCESS:

Intravenous access was done using 16 or 18 Gauge venflon and 10ml/kg intravenous crystalloid was preloaded.

EPIDURAL CATHETERISATION:

With the patient in sitting position under strict aseptic precautions, with 17GTuohy's epidural needle, L3-L4 interspace entered& epidural space identified with loss of resistance technique.

Catheter was secured 3-5 cm inside the epidural space and a test dose of 3 ml of 2% lignocaine was given after negative aspiration of blood and CSF.

STUDY DRUG ADMINISTRATION :

GROUP A : 12 ml of 0.5% Bupivacaine with 60µg Dexmedetomidinein 3ml distlled water.

GROUP B : 12 ml of 0.5% Bupivacaine with 180µg Buprenorphine in 3ml distilled water.

GROUP C: 12 ml of 0.5% Bupivacaine plain with 3 ml of distilled water .

The following observations were made in the patients :

- ✓ Time to T-10 level sensory blockade in minutes.
- ✓ Time to complete motor blockade in minutes.
- ✓ Time to maximum sensory blockade in minutes.
- ✓ Maximum sensory level attained.
- ✓ Time to 2 segmental regression.

- ✓ Motor blockade was assessed before the surgery by using **Bromage Scale.**

- ✓ Sedation score using **Subjective Sedation Scale** and sensory level was assessed every 30 minutes during intraoperative period and hourly postoperatively.

If surgery gets prolonged beyond 3 hours or patient complaints of pain or level descends to T10, 6cc of 0.25% Bupivacaine was given

Inj. Ephedrine 6mg was given when MAP went < 70 mm of Hg

Intra-operatively vitals like **ECG, Spo2, NIBP** were continuously monitored

Postoperatively Patients were shifted to Post Anaesthesia Care Unit (PACU) for monitoring and quality of analgesia assessed by using patient acceptance scale

Rescue analgesia was given on demand with inj.Diclofenac 75 mg i.v, inj.Paracetamol 1g i.v and 0.125% Bupivacaine 6 mlalong with the test drug.

Any adverse effects like vomiting, nausea, pruritis, respiratory depression, headache,dry mouthand shivering were recorded both intraoperatively and postoperatively.

SUBJECTIVE SEDATION SCALE*:*

Grade 0 : awake, conscious

Grade 1 : calm, compose

Grade 2 : awake on command

Grade 3 : awake on gentle tactile stimulus

Grade 4 : awake on vigorous shaking

BROMAGE SCALE :

0 : no block

1 : inability to raise extended leg

2 : inability to flex knee

3 : inability to flex foot

OBSERVATIONS AND RESULTS

STATISTICAL ANALYSIS :

Data was analysed using SPSS software version 15.0 for windows Two sided independent student' s t tests and analysis of variance (ANOVA) with post hoc significance for continuous data, Fisher's exact test and Chi-square test for qualitative data were used. $p<0.05$ was considered as statistically significant and $p<0.001$ as very significant**.**

DEMOGRAPHIC DATA:

The three groups were comparable with respect to their age, weight, sex and ASA Physical status. There was no statistically significant difference among groups in demographic profile.

AGE :

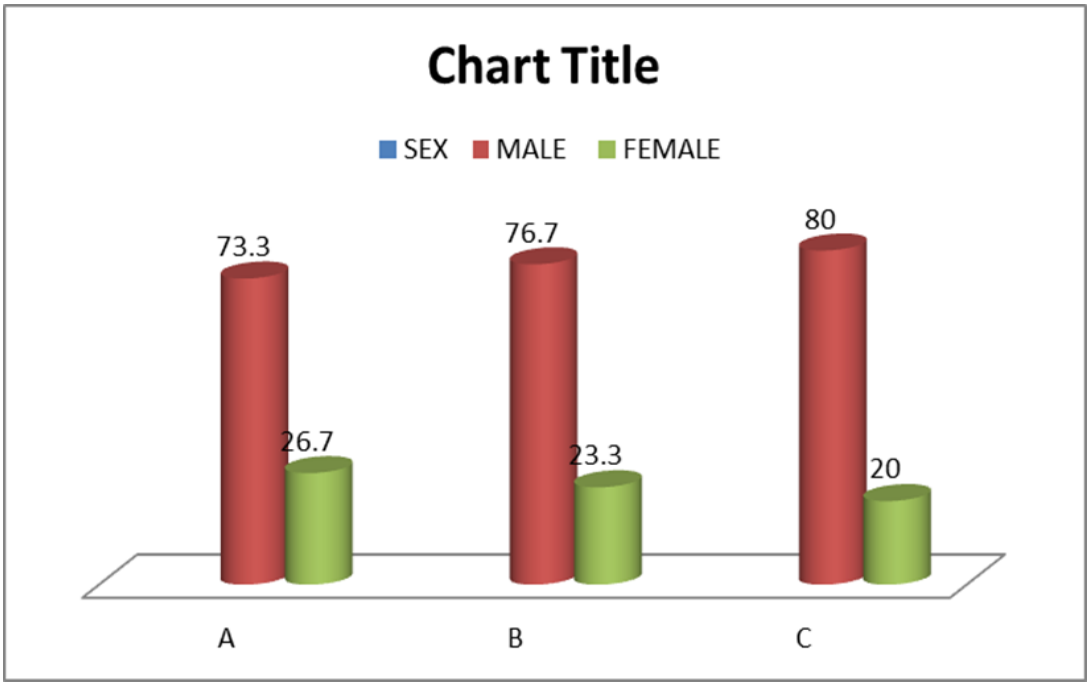
GROUP	A	B	C	P value
Age in years	33.33 ± 7.73	33.83 ± 8.61	33.75 ± 6.28	0.967

WEIGHT :

GROUP	A	B	C	P value
Weight in kgs	**62.7 ± 4.31**	**61.90 ± 3.91**	**63.75 ± 4.166**	**0.305**

SEX :

GROUP	A(%)	B(%)	C(%)	P value
Male	22(73.3%)	23(76.7%)	16(80%)	0.860
Female	8(26.7%)	7(23.3%)	4(20%)	



DURATION OF SURGERY :

GROUP	A	B	C	P value
Duration (in min)	**181 ± 32.73**	**190 ± 33.37**	**178 ± 23.46**	**0.344**

The mean duration of surgery was 181±32.73 min in group A, 190±33.37 min in group B and 178±23.46 min in group C . There was no significant difference in the duration of surgery in all 3 groups (p>0.05)

INITIAL BLOCK CHARACTERISTICS :

Time (in min)	A	B	C	P value
t-T 10	10.60 ± 1.81	11.80 ± 1.49	18.70 ± 1.38	< 0.001
t-max sensory	18.20 ± 2.39	20.40 ± 3.01	19.15 ± 1.75	.005
t-motor	19.80 ± 3.42	30.03 ± 3.60	29.30 ± 2.69	.016

The **onset of analgesia at T 10 dermatomal level** was significantly earlier in group A (10.60±1.81 min), as compared to that of group B (11.80±1.49 min) & group C (18.70±1.38 min) with p value <0.001

Group A > Group B > Group C

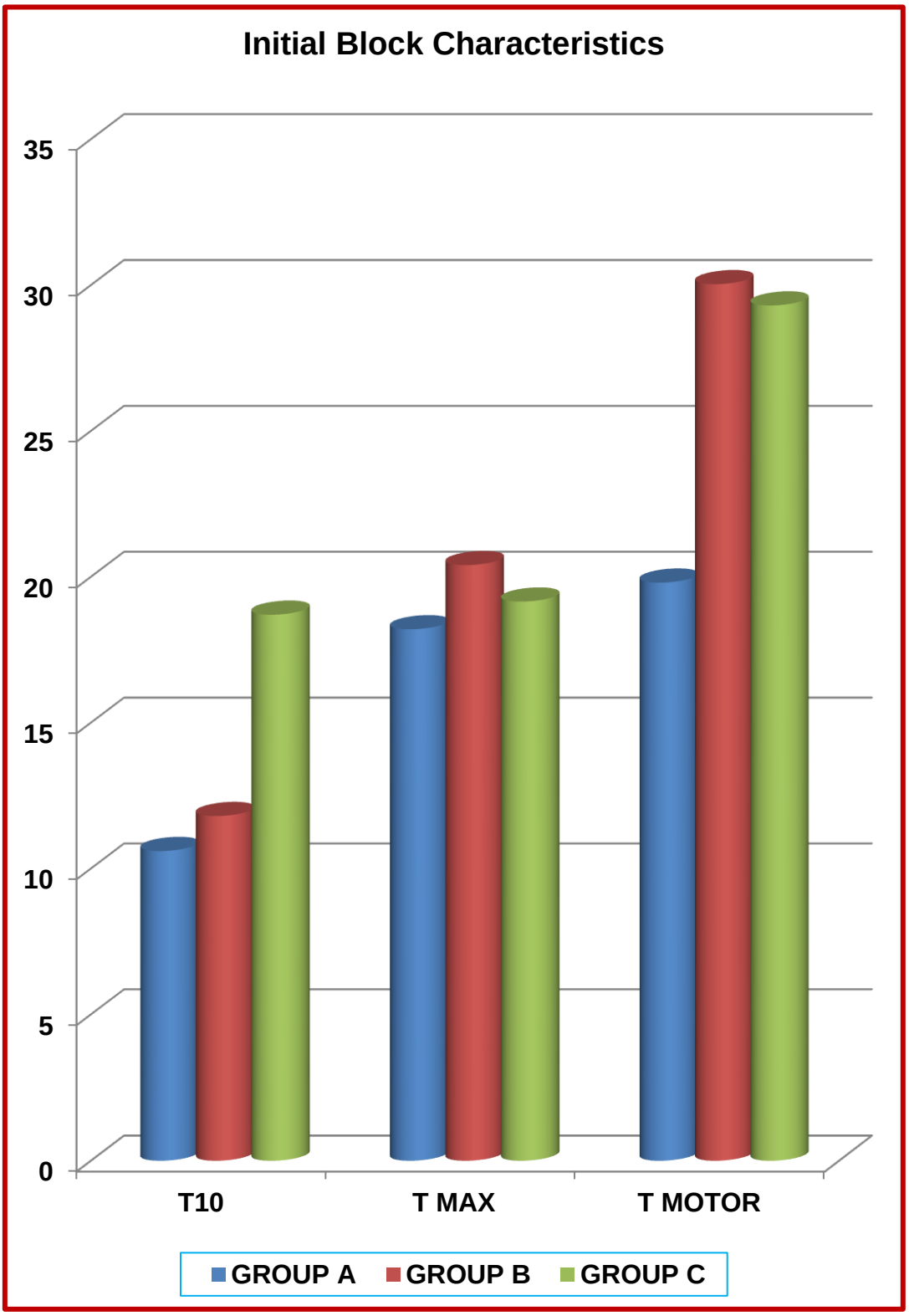
Complete motor blockade was also much earlier in group A (19.80±3.42 min) than group B (30.03±3.60 min) & group C (29.30±2.69 min). There was significant difference between group A with group B (p= 0.01)& group A with group C (p =0.03), but not between group B & group C (p>0.05)

Group A> Group B = Group C

Maximum sensory level was attained earlier in group A (18.20±2.39 min) than that of group B (20.40±3.01min) & group C (19.15±1.75 min) and was significant p = 0.03

Group A > Group C > Group B (spurious)

as the level attained was higher in group B (T6) time taken was more than group C (T8-T10) and was spuriously prolonged than group C


Initial Block Characteristics
35
30
25
20
15
10
5
0
T10
T MAX
T MOTOR
GROUP A
GROUP B
GROUP C

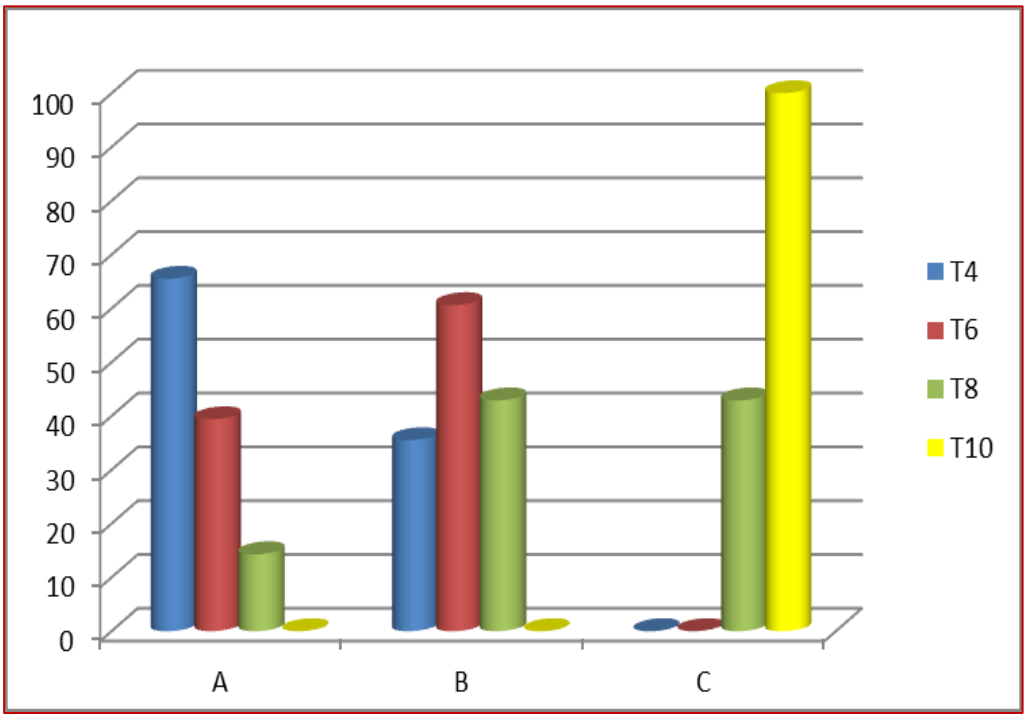
MAXIMUM SENSORY LEVEL :

Max sensory	T4	T6	T8	T10
A(%)	13 (43.3%)	13 (43.3%)	1 (3.3%)	0
B(%)	7 (23.3%)	20 (66.7%)	3 (10%)	0
C(%)	0	0	3 (15%)	17 (85%)

Much higher sensory levels were attained with group A (T4) as compared to (T6) in group B and (T8-T10) in group C .Almost 87% of patients in group A and 90 % of patients in group B attained a level of T4-T6

Group A = Group B > Group C

Maximum sensory level



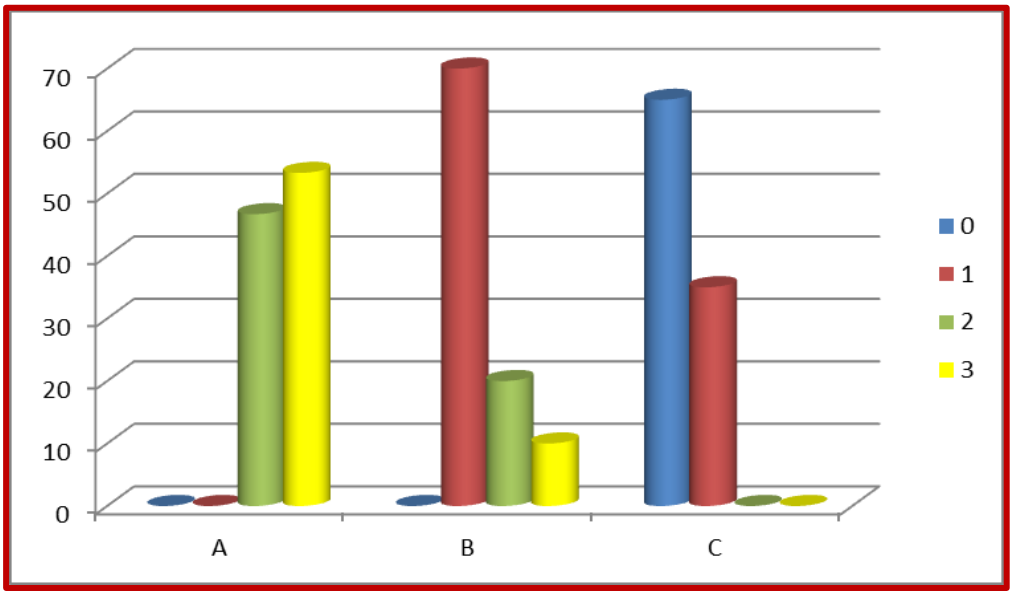
SEDATION SCORE :

Score	A(%)	B(%)	C(%)
0	0	2 (6.7%)	13 (65.5%)
1	0	21 (70%)	7 (35.5%)
2	14 (46.7%)	6 (20%)	0
3	16 (53.3%)	1 (3.3%)	0
4	0	0	0

Mean Sedation scores were stastically higher in group A with p <0.001 than group B & group C .None of the patients in group A were awake during the surgery as compared to group C where more than half of the patients were wide awake. Almost all patients in group A were in deep sleep aroused only on calling or when gently tapped,as compared to nearly two third of patients in group B who were only calm and were awake

Group A > Group B > Group C

Sedation score



POSTOPERATIVE BLOCKCHARACTERISTICS :

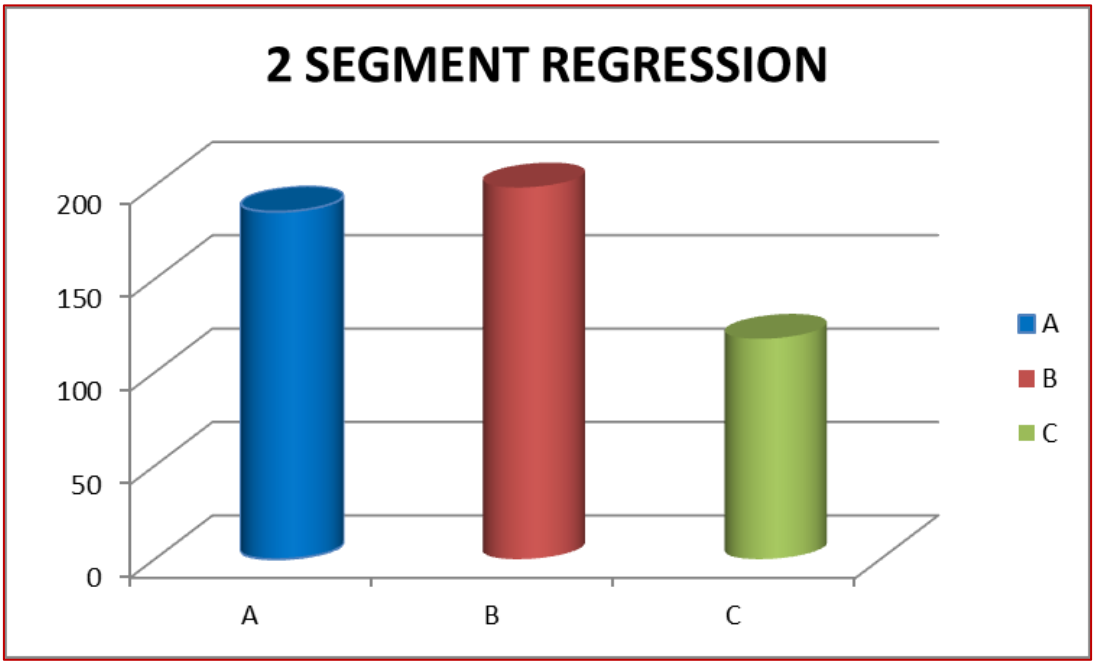
Time (in min)	A	B	C	P value
t-2 segment	186.33 ± 27.23	199 ± 24.82	118.5 ± 18.99	<0.001
t-post op analgesia	410.33 ± 138.99	590.33 ± 140.18	286 ± 48.82	<0.001

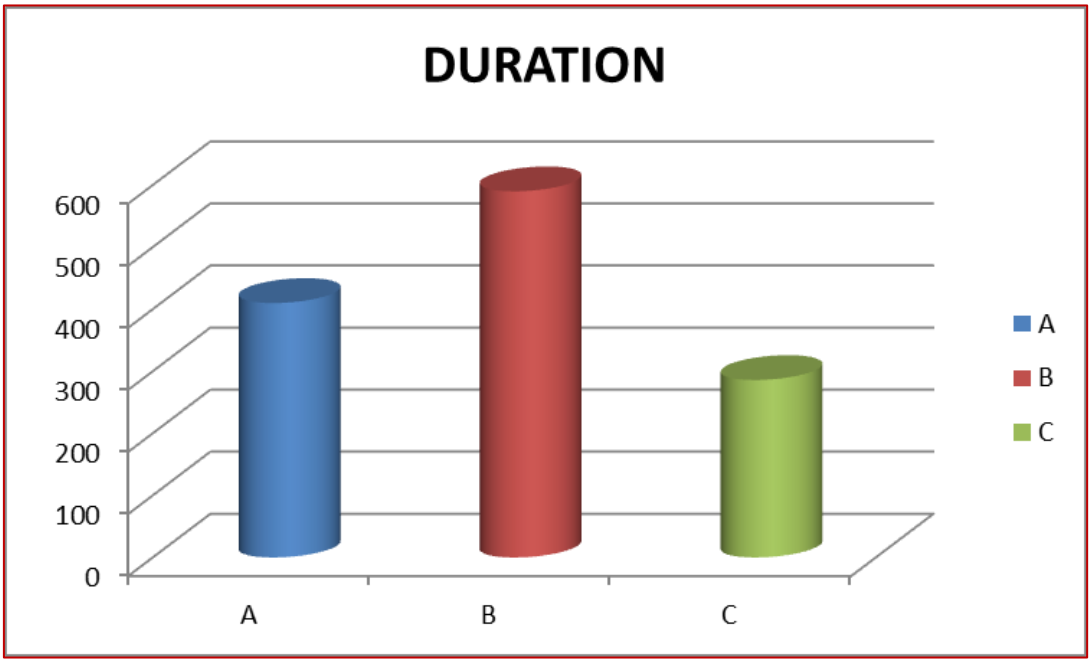
Quality of the blockade during regression was almost similar in group A and group B as the time to two segmental regression (186.33±27.23 min) and (199±24.82 min) respectively was not significant on statistical comparison (p = 0.118) but they were much longer than group C (118.5±18.99 min)

Group A = Group B > Group C

Duration of post operative analgesia was significantly prolonged in group B (590.33±140.18 min) and lasted almost 8-10 hrs postoperatively as compared to (410.33±138.99 min) in group A and a much shorter duration of (286±48.82min) in group C.

Group B > Group A > Group C


2 SEGMENT REGRESSION
200
150
100
50
0
A
B
C
A
B
C

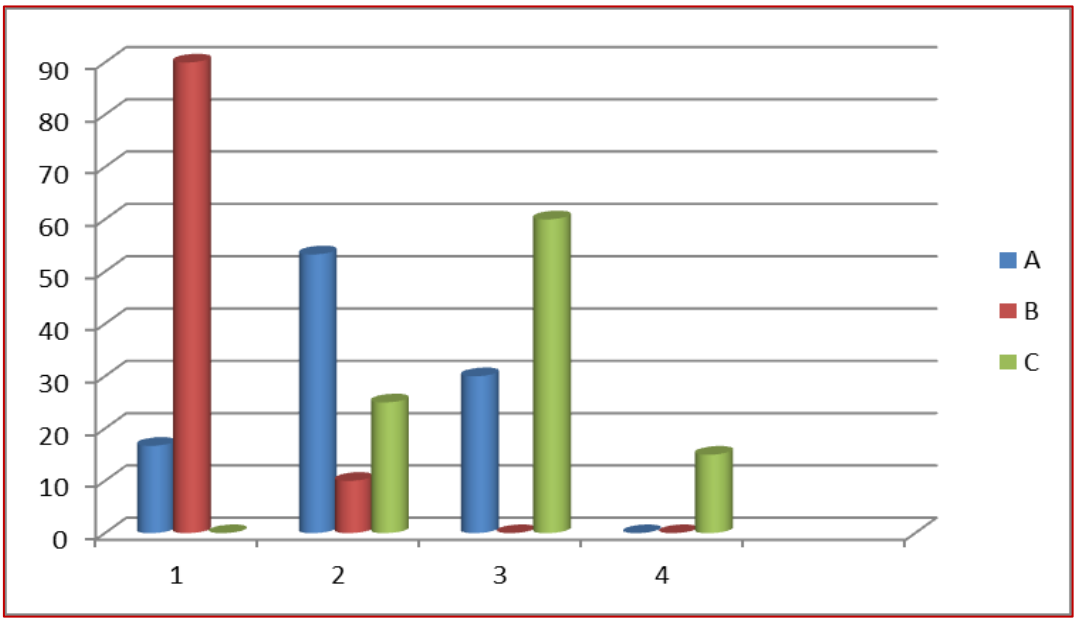

DURATION
600
500
400
300
200
100
0
A
B
C
A
B
C

NUMBER OFPOST OP RESCUE ANALGESIA : (in 24 hrs)

No of rescue analgesia	A (%)	B (%)	C (%)
1	5 (16.7%)	27 (90%)	0
2	16 (53.3%)	3 (10%)	5 (25%)
3	9 (30%)	0	12 (60%)
4	0	0	3 (15%)

Duration of post operative analgesia was significantly prolonged in group B and the quality of analgesia was also good in group B as 90% of patients required rescue analgesia only once in 24 hours as compared to only 16.7% in group A and more than half of the patients in group A required rescue analgesia twice in 24 hours. duration of post operative analgesia was very short in group C as nearly three-fourth of the patients required more than 3 rescue analgesia in the first 24 hours .

Group C > Group A > Group B



INTRA OP HEMODYNAMICS :

Heart rate :

	Group A		Group B		Group C		p value
	mean	**Std.dev**	**mean**	**Std.dev**	**mean**	**Std.dev**	
pr_ base	86.30	6.16	84.20	5.08	85.90	6.15	**0.342**
pr_15	63.13	5.92	86.37	5.90	90.35	6.88	**p value < 0.001**
pr_30	62.93	5.43	79.87	4.65	85.00	5.49	
pr_60	62.90	6.09	78.00	8.06	89.35	11.60	
pr_90	62.83	6.64	76.57	4.72	76.85	10.21	
pr_120	62.87	6.22	74.90	4.10	75.10	7.77	
pr_150	62.93	6.44	75.20	3.95	70.05	8.67	
pr_180	63.20	6.50	75.70	5.42	73.05	7.83	
pr_240	62.17	5.61	76.67	6.27	71.40	6.92	
pr_6hr	62.77	4.74	79.70	8.44	72.20	7.94	
pr_8hr	62.53	5.08	81.37	9.81	70.65	9.18	
pr_10hr	62.00	5.72	80.80	9.30	72.40	8.08	
pr_12hr	62.63	6.63	77.67	7.77	79.70	8.06	
pr_16hr	62.73	5.88	81.37	8.09	70.20	6.23	
pr_20hr	62.17	5.39	79.50	6.81	72.00	6.46	
pr_24hr	72.33	6.70	79.87	5.53	71.35	7.98	

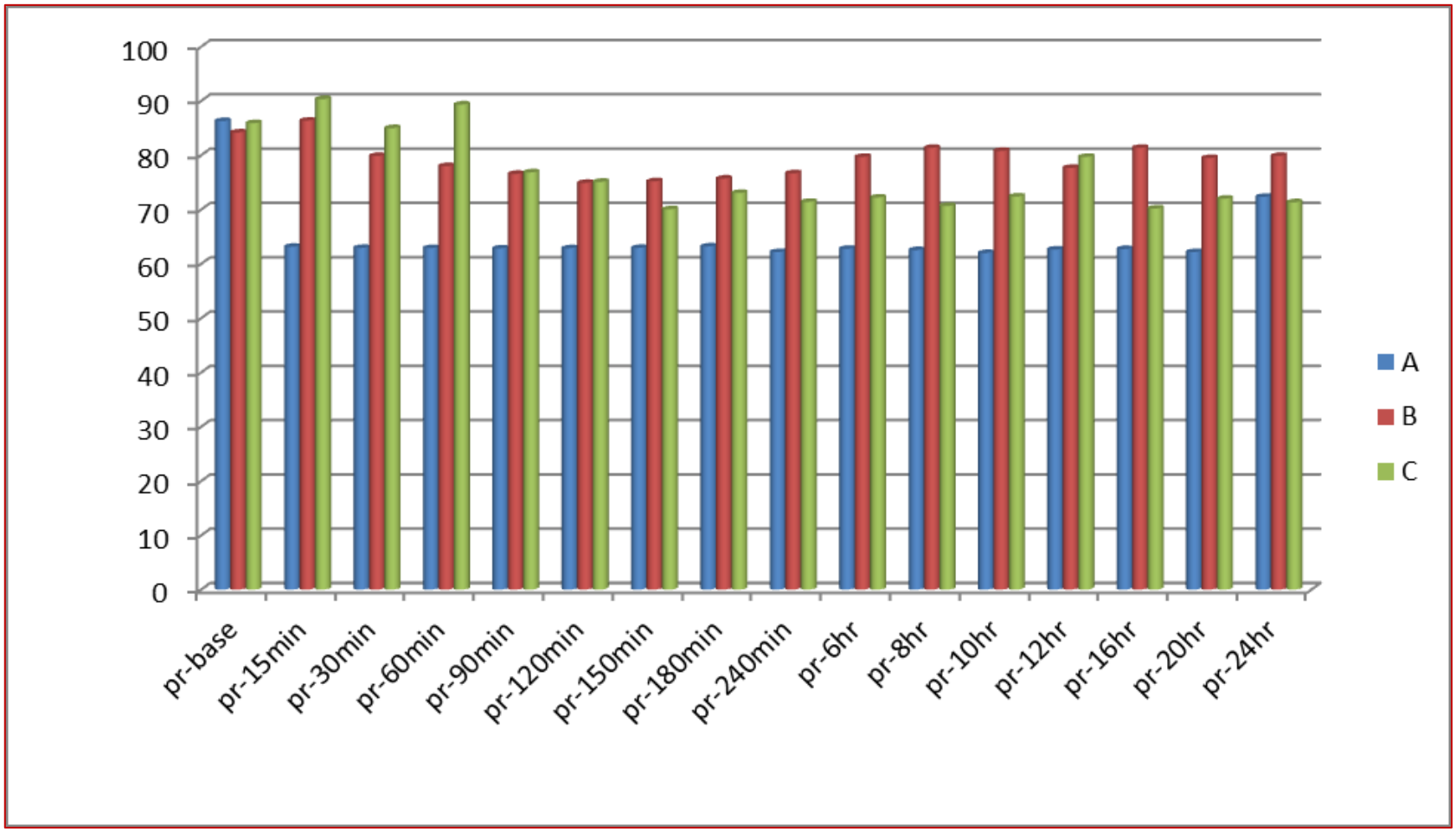
Post hoc significance :

PR – baseline	**Group A**	**Group B**	p = 0.341
		Group C	0.969
	Group B	**Group A**	0.341
		Group C	0.567
PR – 15 min	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	0.071
PR – 30 min	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	0.003
PR – 60 min	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	< 0.001
PR – 90 min	**Group A**	**Group B**	< 0.001
		Group C	<0.001
	Group B	**Group A**	<0.001
		Group C	0.990
PR – 120 min	**Group A**	**Group B**	<0.001
		Group C	<0.001
	Group B	**Group A**	<0.001
		Group C	0.993
PR – 150 min	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	0.339

PR – 180 min	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	0.613
PR –240 min	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	0.865
PR – 6 hr	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	0.613
PR – 8 hr	**Group A**	**Group B**	< 0.001
		Group C	< 0.001
	Group B	**Group A**	< 0.001
		Group C	0.455
PR – 10 hr	**Group A**	**Group B**	< 0.001
		Group C	<0.001
	Group B	**Group A**	<0.001
		Group C	0.990
PR – 12hr	**Group A**	**Group B**	< 0.001
		Group C	<0.001
	Group B	**Group C**	0.554

Base line heart rates were comparable in all groups. There was significant reduction in heart rate in both group A and group B between 15 minutes to 90 minutes, but stabilized afterwards in group B and continued to be around 60/min in group A with a mean heart rate. Even in group A it never went less than 55/min. **Reduction in heart rate** was more in

Group A > Group B >Group C

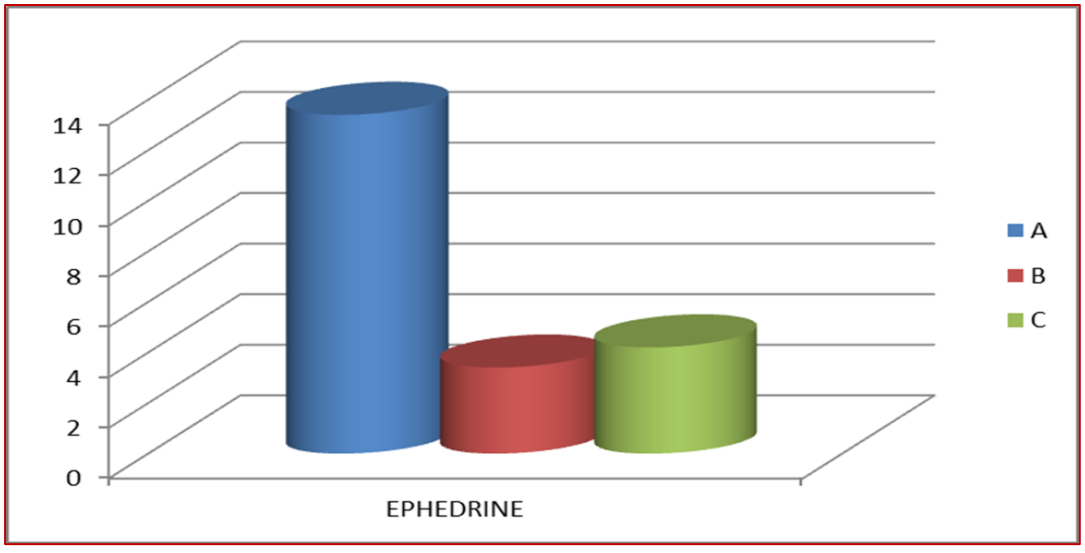

100
90
80
70
60
50
40
30
20
10
0
pr-base
pr-15min
pr-30min
pr-60min
pr-90min
pr-120min
pr-150min
pr-180min
pr-240min
pr-6hr
pr-8hr
pr-10hr
pr-12hr
pr-16hr
pr-20hr
pr-24hr
A
B
C

Requirement of ephedrine (in mgs) :

GROUP	A	B	C	P value
Ephedrine used (in mgs)	13.4±6.99	3.4±5.15	4.2±3.92	<0.001
Lowest MAP (in mm of Hg)	67.17±5.45	70.17±4.62	69.7±5.44	0.027

Overall hemodynamics was stable in all 3 groups , as the Mean Arterial Pressure (MAP), never went below 60 mm of Hg throughout the perioperative period. But **the requirement of Inj.Ephedrine** was significantly higher in group A ($p<0.001$), there was no stastistical difference in requirement of ephedrine between group B and group C ($p=0.877$)

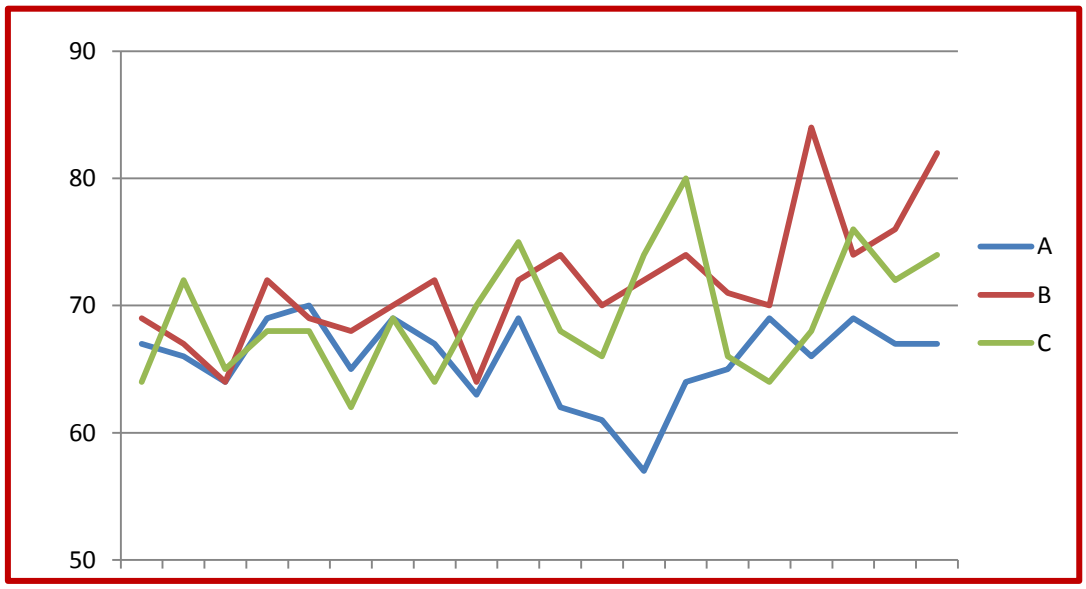
Group A > Group B = Group C



The lowest MAP(mean arterial pressure) attained was in group A (67.17±5.45 mm of Hg) and was always on the low normal side in group A when compared to group B and group C where the MAP remained stable around (70.17±4.62 mm of Hg) and (69.7±5.44 mm of Hg) respectively. Thus the **mean arterial pressure** maintained at a better level in group B

GROUP B =GROUP C> GROUP A

Lowest mean arterial pressure



PATIENT ACCEPTANCE :

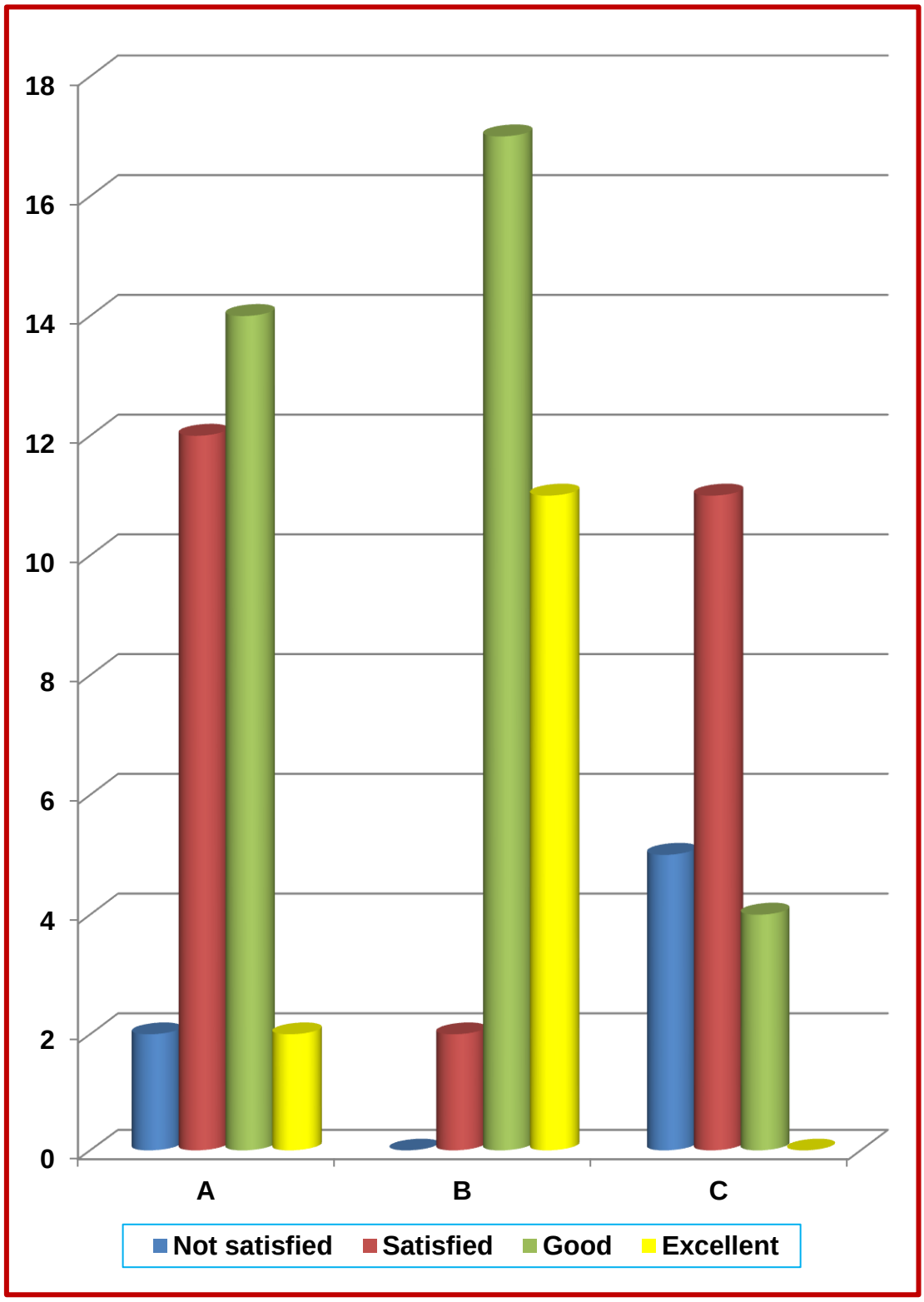
Group	0 Not satisfied	1 satisfied	2 good	3 excellent	p value
A	2(8%)	12(40%)	14(46%)	2(8%)	
B	0	2(8%)	17(60%)	11(38%)	
C	5(20%)	11(54%)	4(16%)	0	**<0.001**

Patient acceptance was significantly better in group B, as 60% of patient rated is as good and 38% as excellent as compared to only 46% and 8% in group B rated it as good and better respectively.

Patient acceptance in group B was highly significant than group A ($p<0.001$) and group C ($p< 0.001$). therewas no significant difference between group A and group C in patient acceptance.($p = 0.0667$)

Group B>Group A =Group C

PATIENT ACCEPTANCE SCALE



ADVERSE EFFECTS :

GROUP	A	B	C	P value
HEADACHE	2(8%)	4(16%)	2(10%)	0.667
NAUSEA	0(0%)	2(8%)	2(10%)	0.489
VOMITING	0(0%)	2(8%)	2(10%)	0.489
DRY MOUTH	3(10%)	0(0%)	0	0.109
RESPIRATORY DEPRESSION	0(0%)	0(0%)	0	1.000
SHIVERING	0	3(10%)	4(20%)	0.667

Adverse effect profiles were comparable in all 3 groups. side effects like nausea, vomiting, headache, dry mouth and shivering was observed in all 3 groups and were statically insignificant with $p>0.05$, no respiratory depression or bradycardia i.e., PR< 50/min was observed.

DISCUSSION

Traditionally opioids are used as adjuvants in epidural and spinal anaesthesia. Alpha 2 agonist like Clonidine was also successfully used as adjuvant in the last decade as it produced excellent sedation and analgesia, but it also produced severe hypotension and bradycardia to overcome this newer alpha 2 agonist Dexmedetomidine was introduced and number of studies have been conducted successfully with Dexmedetomidine as adjuvant for both spinal and epidural blockade. Buprenorphine a long acting partial agonist, is a time honoured drug well known for its prolonged analgesic action but has a theoretical side effect of respiratory depression. Number of studies have also been conducted to elicit the safety and excellent analgesia produced by buprenorphine. Keeping in mind the side effect profile of both the drugs we carefully designed a study to extract the maximum out of these 2 drugs as epidural adjuvants avoiding side effects.

A total of 80 patients who underwent elective lower limborthopaedic surgeries were randomly allocated in 3 groups.

GROUP A (30) : 12 ml of 0.5% Bupivacaine with 60µg Dexmedetomidine in 3ml distilled water .

GROUP B (30) : 12 ml of 0.5% Bupivacaine with 180µg Buprenorphine in 3ml distilled water .

GROUP C (20) : 12 ml of 0.5% Bupivacaine plain with 3 ml of distilled water .

The demographic profile in all 3 groups were similar and there was no significant difference in Age, Sex, ASA physical status and Weight. Duration of surgery was around 3 hours in all 3 groups.

ONSET OF BLOCK :

Both Dexmedetomidine and Buprenorphine enabled an earlier onset and establishment of analgesia. Initial block characteristics were favourable in Dexmedetomidine than Buprenorphine group. Group A patients not only had an earlier onset of sensory block at T10 but a much higher dermatome level of blockade and complete motor blockade in a shorter duration. The addition of these two adjuvants promotes faster onset as compared to time of onset of sensory analgesia with Bupivacaine alone.

This could be correlated with a study by Sukhminder et al where they compared Dexmedetomidine1mcg/kg and Fentanyl 1mcg/kg along with 15 ml of 0.75% epidural Ropivacaine in lower limb surgeries in which the onset was significantly earlier than Fentanyl. In another study conducted by Sukhminder et al epidural Dexmedetomidine 2 mcg/kg was compared with clonidine 2 mcg/kg along with 17 ml of 0.75% Ropivacaine in which also onset was earlier than Clonidine.

SEDATION:

Dexmedetomidine produced better sedation than Buprenorphine as most patients were deep asleep and arousable only on command or gentle tapping and without any respiratory depression. Patients in buprenorphine group remained calm and campose but were awake .

This could be correlated to

1. Sukhminder et al., in 2 studies that Dexmedetomidine produced sedation of grade 3 when compared with Clonidine and Fentanyl
2. Vijay.G. anand et al in his study observed that caudal Dexmedetomidine 1mcg/kg along with 0.25% Bupivacaine produced excellent sedation in pediatrics without respiratory depression

DURATION OF ANALGESIA :

Duration of analgesia was significantly prolonged in Buprenorphine group than the other 2 groups. Patients in Buprenorphine groups did not require rescue analgesia for more than 8 hours post op as compared to 4-6 hours in Dexmedetomidine group and 2-3 hours in plain bupivacaine group . group B patients also required lesser Number of postoperative rescue analgesia and patient acceptance was also better with the quality of analgesia produced in group B than group A and group C

This could be correlated with

1. Kiran agarwal et al., observed that the duration of postoperative analgesia after injection of 0.125% Bupivacaine with 0.075 mg of Buprenorphine was 690±24 minutes.

2. Lanz et al ., observed that postoperative analgesia was prolonged to more than 9.6±3.2 hours in patients who received 0.3mg of epidural Buprenorphine , 7.5±4.2hours in patients who received 0.15mg of Buprenorphine

HEMODYNAMIC STABILITY :

Overall hemodynamics were stable in all 3 groups , as MAP never went **below 60 mm of Hg** and pulse rate never went less than **50/min.** But the requirement of Ephedrine was significantly higher in Dexmedetomidine group and the blood pressure remained on the lower side in group A. Blood Pressure was stable in group B and C and requirement of Ephedrine was also meagre. Hypotension was more with group A.

This was against the observations in Sukhminder et al comparative efficacy of epidural Dexmedetomidine vs Fentanyl with Ropivacaine. As requirement of Vasopressors was not significantly higher when compared to

Fentanyl, most probably due to the use of Ropivacaine which causes less hemodynamic changes than Bupivacaine .

ADVERSE EFFECTS :

None of the patients had respiratory difficulty warranting active management and the side effect profile in all 3 groups were not significant which correlated well with all other studies.

We observed a slightly higher incidence of nausea and vomiting in group B, than group A and C. Dry mouth was observed in Dexmedetomidine group and there was no shivering in group A.As the patients were catheterized urinary retention could not be assessed.

SUMMARY

This double blinded prospective randomized controlled study was done to evaluate the Duration of Analgesia, Hemodynamic Stability, Sedation and Adverse effects of Dexmedetomidine and Buprenorphine as adjuvants to 0.5% epidural Bupivacaine in patients undergoing lower limb orthopaedic surgeries.

The following observations were made:

1. Addition of Dexmedetomidine and Buprenorphine significantly shortens the onset of analgesia and increases the maximum level of blockade.

2. Addition of Dexmedetomidine produces arousable intraoperative sedation than Buprenorphine.

3. Addition of Buprenorphine prolongs the duration of analgesia post operatively and maintains better hemodynamic stability

4. Quality of postoperative analgesia, number of rescue analgesia needed and patient acceptance was better with Buprenorphine.

5. There was no respiratory depression for both drugs and the incidence of side effects were statistically insignificant between groups.

CONCLUSION

To conclude that 180µg of Buprenorphine seems to be a better adjuvant to epidural bupivacaine (0.5%) than 60µg Dexmedetomidine for postoperative analgesia. It has an excellent quality and a prolonged duration of postoperative analgesia with minimal side effects. The hemodynamic stability was well maintained with Buprenorphine. Even though 60µg Dexmedetomidine produced early onset of analgesia and good sedation, duration of postoperative analgesia was shorter and fluctuations in hemodynamics were significantly higher.

Overall experience with Buprenorphine was satisfactory as compared to Dexmedetomidinebecause of its superior quality of analgesia, better hemodynamics and patient comfort.

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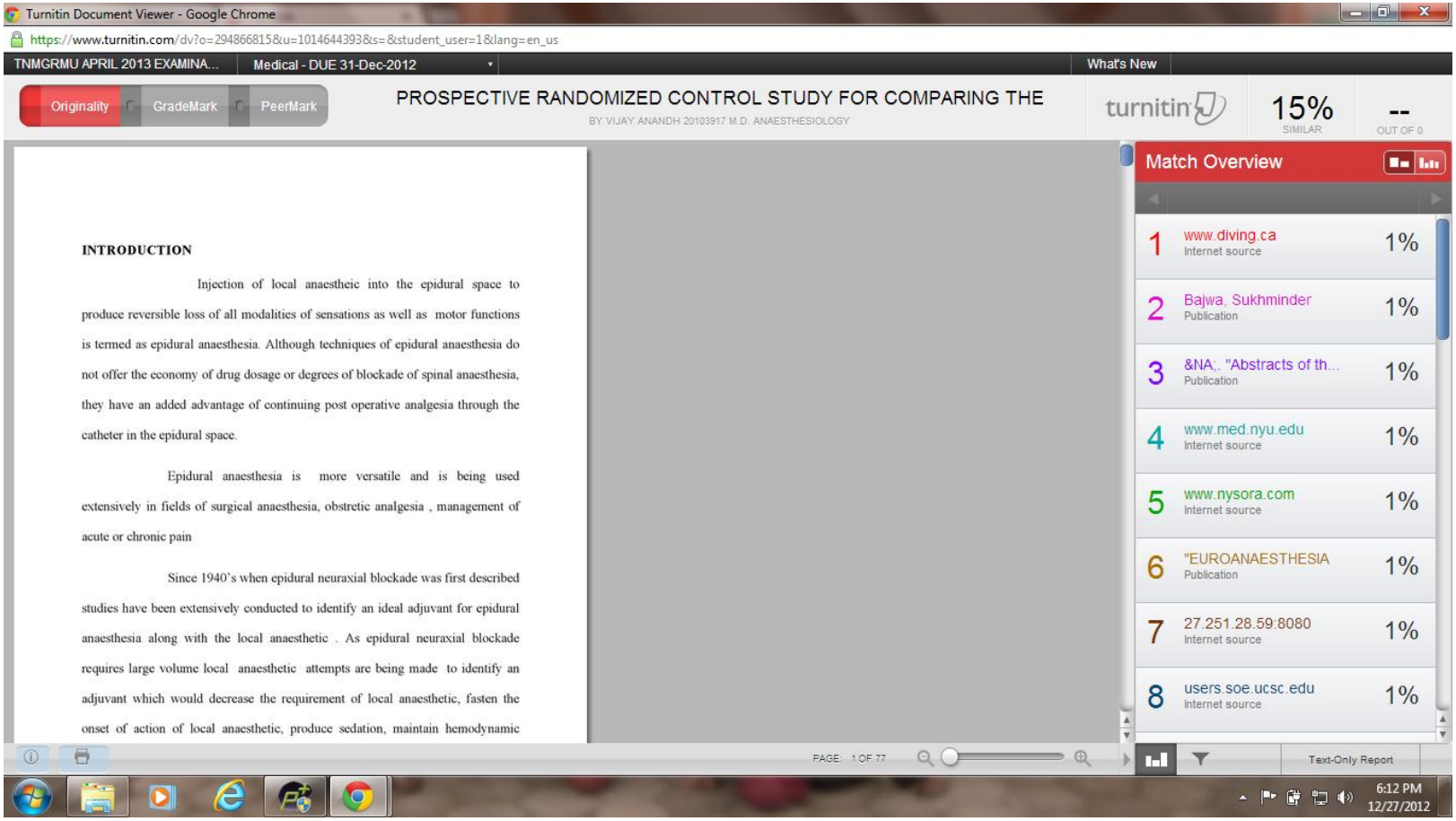
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INTRODUCTION
Injection of local anaestheic into the epidural space to produce reversible loss of all modalities of sensations as well as motor functions is termed as epidural anaesthesia. Although techniques of epidural anaesthesia do not offer the economy of drug dosage or degrees of blockade of spinal anaesthesia, they have an added advantage of continuing post operative analgesia through the catheter in the epidural space.
Epidural anaesthesia is more versatile and is being used extensively in fields of surgical anaesthesia, obstretic analgesia , management of acute or chronic pain
Since 1940's when epidural neuraxial blockade was first described studies have been extensively conducted to identify an ideal adjuvant for epidural anaesthesia along with the local anaesthetic . As epidural neuraxial blockade requires large volume local anaesthetic attempts are being made to identify an adjuvant which would decrease the requirement of local anaesthetic, fasten the onset of action of local anaesthetic, produce sedation, maintain hemodynamic
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PATIENT CONSENT FORM

Study title : Prospective randomised control study for comparing the efficacy of epidural buprenorphine and dexmedetomidine with 0.5% bupivacaine in lower limborthopaedic surgeries.

Study centre : Institute of Anaesthesiology and Critical Care, Rajiv Gandhi Govt. Hospital, Chennai.

Participant name : **Age:** **Sex:**

I.P.No:

I confirm that i have understood the purpose of procedure for the above study .i have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety,advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that i am free to withdraw at anytime without giving any reason.

I understand that investigator ,regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if i withdraw from the study . I understand that my identity will not be revealed in any information released to third parties or published , unless as required under the law . I agree not to restrict the use of any data or results that arise from the study .

Time:
Date: **Signature / thumb impression**
Place: **Patient name:**

Signature of the investigator:

Name of the investigator:

INFORMATION TO PARTICIPANTS

Investigator : **Dr.S.VIJAY ANANDH** .

Name of the Participant :

Title : **PROSPECTIVE RANDOMISED CONTROL STUDY FOR COMPARING THE EFFICACY OF EPIDURAL BUPRENORPHINE AND DEXMEDETOMIDINE WITH 0.5% BUPIVACAINE IN LOWER LIMB ORTHOPAEDIC SURGERIES .**

You are invited to take part in this research study. We have got approval from the IEC. Your are asked to participate because you satisfy the eligibility criteria .We want to compare and study the safety and efficacy of epidural buprenorphine and dexmedetomidine with 0.5% bupivacaine in lower limb surgeries

What is the Purpose of the Research:

For orthopaedic surgeries , spinal/ epidural anaesthesia with 0.5% bupivacaine alone is commonly given during anaesthesia which results in greater hemodynamic instability and short duration of pain relief . This study compares the hemodynamic changes in different doses of spinal bupivacaine in combined spinal epidural technique.

The Study Design:

All the patients in the study will be divided into three groups. Epidural catheter will be placed at L3-L4 in all patient . group A will receive 0.5% bupivacaine with dexmedetomidine,group B will receive 0.5% bupivacaine with buprenorphine,group C will receive 0.5% bupivacaine with distilled water . Time of onset of sensory and motor blockade noted. Surgery proceeded and all patients are shifted to PACU postoperatively for observation and postoperative pain relief management.

Benefits:

In pure epidural technique there is less hemodynamic instability. Moreover, the epidural catheter can be used for post-operative pain relief also.

Discomforts and risks:

Reduction in heart rate and blood pressure can occur. Sometimes vomiting can occur. Reduction in heart rate is managed with inj. Atropine. Reduction in blood pressure is managed with inj. Ephedrine. Inj.Ondansetron is given pre-operatively to control vomiting.

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative of setting the standard treatment and your safety is our prime concern.

Time :

Date :

Place : **Signature / Thumb Impression**

Patient name :

Signature of the Investigator : _____

Name of the Investigator : _____

PROFORMA

Name: **Age:** **Sex:** **Wt:** **Ip No:**

Diagnosis: **ASA:**

Plan:

Time to T10 blockade (in min)		**Rescue analgesia**
Maximum sensory level		
Time to max sensory level (in min)		**Adverse effects**
Time to complete motor blockade (in min)		
Time to 2 segmental regression (in min)		
Duration of sensory block		
Sedation score		

Sedation scale:

Grade 0 :awake,conscious

Grade 1 :calm,compose

Grade 2 : awake on command

Grade 3 : awake on gentle tactile stimulus

Grade 4 : awake on vigorous shaking

Bromagescale :

0 : no block

1 : inability to raise extended leg

2 : inability to flex knee

3 : inability to flex foot

TIME	BP	PR	Spo2	RR	IVF	DRUGS	MAP

MASTER CHART

S. NO	NAME	AGE	SEX	DIAGNOSIS	PROCEDURE	WEIGHT	ASA
GROUP - A							
1.	VENKATESH	18	M	avascular necrosis Lt hip	Lt THR	55	1
2.	RAVI	22	M	# Rt SHAFT OF FEMUR	ORIF	60	1
3.	MURUGAN	42	M	# NECK OF FEMUR	HEMIARTHROPLASTY	58	2
4.	KATHAVARAYAN	40	M	# SHAFT OF FEMUR	ORIF	68	1
5.	JITHENDRA	31	M	# Lt ACETABULUM	ORIF	60	1
6.	KANNAN	31	M	# BB Rt LEG	ORIF	58	1
7.	VILLALAN	41	M	OSTEOARTHRITIS Lt HIP	Lt THR	60	1
8.	RAVI	39	M	# SHAFT OF FEMUR	ORIF	62	1
9.	PARIMALA	30	F	# NECK OF FEMUR	ORIF	60	1
10.	VISHNU	24	M	# SHAFT OF FEMUR	HEMIARTHROPLASTY	66	1
11.	VIGNESH	23	M	# Lt ACETABULUM	ORIF	70	1
12.	VIJAYAN	30	M	# SHAFT OF FEMUR	ORIF	65	1
13.	PRABAKAR	29	M	# SHAFT OF FEMUR	ORIF	66	1
14.	ESHWARI	45	F	OSTEOARTHRITIS Lt HIP	THR	70	1
15.	PRIYA	29	F	# NECK OF FEMUR	THR	65	1
16.	SAMPATH	44	M	# BB Rt LEG	ORIF	66	1
17.	SELVAKUMAR	40	M	avascular necrosis Lt hip	THR	62	1
18	BABLOO GUPTA	28	M	# Lt ACETABULUM	ORIF	60	1
19.	JYOTHI	33	F	# SHAFT OF FEMUR	ORIF	66	1
20.	ALBERT	34	M	# MEDIAL CONDYLE FEMUR	ORIF	56	1
21.	SURESH	35	M	OSTEOARTHRITIS Rt HIP	THR	70	1
22	AMBIKA	45	F	# NECK OF FEMUR	HEMIARTHROPLASTY	65	1
23.	RAMANUJAM	25	M	# BB Rt LEG	ORIF	66	1
24.	PRAKASH	33	M	OSTEOARTHRITIS Lt hip	THR	62	1
25.	PUSHPA	34	F	# BB Rt LEG	ORIF	60	1
26.	HARIKRISHNAN	28	M	# NECK OF FEMUR	HEMIARTHROPLASTY	58	2
27.	MAYAVATHI	45	F	# SHAFT OF FEMUR	ORIF	68	1
28.	RAMESH	44	M	#BB Lt LEG	ORIF	60	1
29.	SANJAY	24	M	# BB Rt LEG	ORIF	58	1
30.	CHITRA	34	F	# TIBIAL PLATEAU	BICOLUMNAR PLATING	60	1

MASTER CHART

S. NO	NAME	AGE	SEX	DIAGNOSIS	PROCEDURE	WEIGHT	ASA
GROUP - B							
1.	RAVI	42	M	#NON UNION TIBIA	ILIZAROV'S FIXATION	65	1
2.	RAMESH	34	M	# SHAFT OF FEMUR	ORIF	56	1
3.	BAJRANG CHONDI	40	M	#SHAFT OF FEMUR,PATELLA	ORIF & WIRING	60	1
4.	KRISHNAN	52	M	# BB Lt LEG	ORIF	60	2
5.	ESTHER	48	F	# BB Lt LEG	ORIF	60	1
6.	MOHANA	35	F	# SHAFT OF FEMUR	ORIF	58	1
7.	ASPADHAM	20	M	# PROXIMAL TIBIA	ORIF	65	1
8.	VENKATESAN	28	M	#BB Rt LEG	ORIF	68	1
9.	VENU	45	M	# TROCHANTER Lt FEMUR	DHS	62	1
10.	SIVAKUMAR	27	M	#SHAFT OF FEMUR,PATELLA	ORIF & WIRING	58	1
11.	SUNDAR	29	M	# SHAFT OF FEMUR	ORIF	60	1
12.	BABU	41	M	# SHAFT OF FEMUR	ORIF	70	1
13.	SUDHAKAR	26	M	#BB Rt LEG	ORIF	64	1
14.	MURUGAN	26	M	# DISTAL TIBIA	ORIF	65	1
15.	PONNAN	35	M	SEGMENTAL # TIBIA	ILIZAROV'S FIXATION	56	1
16.	SURESH	18	M	#SHAFT OF FEMUR,PATELLA	ORIF & WIRING	64	1
17.	CHANDRAN	24	M	#MEDIAL MALLEOLUS TIBIA	ORIF	60	1
18.	CHELLAMUTHU	27	M	# PROXIMAL TIBIA	ORIF	70	1
19.	CHINNADURAI	27	M	#NON UNION TIBIA	ILIZAROV'S FIXATION	62	1
20.	RAJENDRAN	34	M	#BB Rt LEG	ORIF	64	1
21.	MANJULA	33	F	# SHAFT OF FEMUR	ORIF	60	1
22.	KUMAR	40	M	# SHAFT OF FEMUR	ORIF	60	2
23.	LAKSHMI	41	F	#BB Rt LEG	ORIF	60	1
24.	KUPPAMAL	45	F	# DISTAL TIBIA	ORIF	58	1
25.	VASANTH	28	M	# TROCHANTER Lt FEMUR	DHS	62	1
26.	RAJALAKSHMI	33	F	#SHAFT OF FEMUR,PATELLA	ORIF & WIRING	58	1
27.	MAHESH	26	M	# SHAFT OF FEMUR	ORIF	60	1
28.	RAJESHWARI	44	F	# SHAFT OF FEMUR	ORIF	70	1
29.	MANIKANDAN	28	M	OSTEOARTHRITIS Lt HIP	Lt THR	60	1
30.	MUTHU	39	M	# SHAFT OF FEMUR	ORIF	62	1

MASTER CHART

S. NO	NAME	AGE	SEX	DIAGNOSIS	PROCEDURE	WEIGHT	ASA
GROUP - C							
1.	VARATHARAJAN	40	M	# SHAFT OF FEMUR	ORIF	68	1
2.	ARUN	31	M	# Lt ACETABULUM	ORIF	60	1
3.	VANITHA	31	M	# BB Rt LEG	ORIF	58	1
4.	VIJAY	41	M	# BB Rt LEG	ORIF	60	1
5.	SELVI	39	M	# SHAFT OF FEMUR	ORIF	62	1
6.	ANANDH	30	F	# NECK OF FEMUR	ORIF	60	1
7.	PUNITHA	24	M	# SHAFT OF FEMUR	HEMIARTHROPLASTY	66	1
8.	VASUDEVAN	23	M	# Lt ACETABULUM	ORIF	70	1
9.	SUBBHARAO	30	M	# SHAFT OF FEMUR	ORIF	65	1
10.	MITHUN	29	M	# SHAFT OF FEMUR	ORIF	66	1
11.	BASKAR	45	F	#BB Rt LEG	ORIF	70	1
12	ESHWARAIAH	29	F	# DISTAL TIBIA	ORIF	65	1
13.	BAKKIYARAJ	44	M	# BB Rt LEG	ORIF	66	1
14.	SUNIL KUMAR	40	M	#MEDIAL MALLEOLUS TIBIA	ORIF	62	1
15.	SENTHIL	28	M	# Lt ACETABULUM	ORIF	60	1
16.	SABAPATHY	33	F	# SHAFT OF FEMUR	ORIF	66	1
17.	YESHWANTH	34	M	# MEDIAL CONDYLE FEMUR	ORIF	56	1
18.	SARAVANAN	35	M	# BB Rt LEG	ORIF	70	1
19.	MOHAMED ALI	38	M	#BB Lt LEG on EXFIX	EXCHANGE NAILING	65	1
20.	SANTHOSH	31	M	INFECTED IMPLANT TIBIA	IMPLANT REMOVAL	60	1

MASTER CHART

S. No	t-T10	t-sensory	t-motor	max sensory	t-2 segment regression	Duration of analgesia	Sedation score	Ephedrine used	Lowest MAP	Duration of surgery	Intra op EPIDURAL top up	post op rescue	Patient acceptance score
GROUP - A													
1.	13	20	26	T6	160	250	2	18	67	190	0	2	1
2.	13	22	24	T6	180	300	3	18	66	260	0	2	3
3.	11	20	22	T6	150	420	3	0	90	140	0	2	2
4.	11	18	20	T4	180	540	2	12	69	180	0	2	2
5.	12	20	24	T6	160	275	2	0	76	180	0	3	1
6.	14	20	25	T6	150	335	3	6	65	120	0	2	1
7.	12	20	24	T6	240	710	2	6	69	180	0	1	2
8.	12	19	18	T4	200	490	3	12	67	190	0	2	2
9.	9	18	20	T4	210	530	3	18	63	180	0	2	3
10.	12	18	18	T8	200	600	2	24	69	190	0	1	2
11.	11	19	20	T6	170	660	2	6	62	200	0	1	2
12.	9	18	18	T5	180	440	3	24	61	200	0	3	2
13.	12	20	18	T4	180	420	3	30	57	240	0	2	1
14.	10	16	18	T5	210	380	2	12	64	150	0	2	1
15.	8	15	18	T4	150	180	3	18	65	160	0	3	1
16.	9	14	16	T6	210	300	3	18	69	170	0	2	1
17.	9	14	15	T4	210	380	3	18	66	150	0	3	2
18.	8	18	15	T4	200	510	2	12	69	230	0	2	0
19.	9	20	20	T4	180	660	3	18	67	160	0	1	1
20.	10	22	18	T4	210	280	2	6	67	160	0	3	2
21.	10	16	18	T5	210	380	2	12	64	180	0	3	2
22.	8	15	18	T4	150	180	3	18	65	120	0	3	1
23.	9	14	16	T6	210	300	3	18	69	180	0	2	2
24.	9	14	15	T4	210	380	3	18	66	210	0	3	2
25.	8	18	15	T4	200	360	2	12	69	240	0	2	1
26.	11	20	22	T6	150	420	3	12	65	180	0	2	0
27.	11	18	20	T4	180	480	2	12	69	150	0	2	2
28.	12	20	24	T6	160	275	2	12	66	170	0	3	1
29.	14	20	25	T6	150	335	3	6	65	190	0	2	1
30.	12	20	24	T6	240	540	2	6	69	180	0	1	2

MASTER CHART

S. No	t-T10	t-sensory	t-motor	max sensory	t-2 segment regression	Duration of analgesia	Sedation score	Ephedrine used	Lowest MAP	Duration of surgery	Intra op EPIDURAL top up	post op rescue	Patient acceptance score
GROUP - B													
1.	14	18	20	T6	200	660	0	6	69	240	0	1	2
2.	10	20	20	T6	210	360	2	6	67	210	0	2	2
3.	10	15	18	T4	200	600	1	18	64	220	0	1	2
4.	12	22	25	T4	220	720	2	0	72	220	0	1	3
5.	13	20	24	T6	180	540	1	6	69	190	0	1	3
6.	13	25	22	T6	240	600	2	6	68	180	0	1	2
7.	15	20	25	T6	200	360	1	0	70	270	0	1	2
8.	11	18	220	T6	180	480	1	0	72	240	0	1	3
9.	9	18	18	T4	200	720	1	6	64	150	0	1	2
10.	13	24	28	T6	180	480	1	0	72	180	0	1	3
11.	13	25	25	T6	200	680	1	0	74	180	0	1	2
12.	12	20	25	T8	160	780	1	0	70	200	0	1	2
13.	12	24	28	T6	180	300	1	0	72	180	0	2	3
14.	10	18	24	T6	180	450	1	0	74	120	0	1	3
15.	11	18	28	T8	200	600	1	0	71	170	0	1	3
16.	12	18	24	T6	240	720	1	0	70	210	0	2	3
17.	13	20	28	T6	180	360	1	0	84	120	0	1	2
18.	10	18	22	T6	240	480	1	0	74	180	0	1	1
19.	10	18	22	T6	210	740	1	0	76	150	0	1	2
20.	12	25	28	T6	150	760	0	0	82	210	0	1	2
21.	10	15	18	T4	200	600	1	18	64	220	0	1	1
22.	12	22	25	T4	220	720	2	0	72	220	0	1	2
23.	13	20	24	T6	180	540	1	6	69	190	0	1	2
24.	13	25	22	T6	240	600	2	6	68	180	0	1	3
25.	9	18	18	T4	200	720	1	6	64	150	0	1	2
26.	13	24	28	T6	180	480	1	0	72	180	0	1	3
27.	13	25	25	T6	200	680	1	0	74	180	0	1	2
28.	12	20	25	T8	160	780	1	0	70	200	0	1	2
29.	12	20	24	T6	240	710	2	6	69	180	0	1	3
30.	12	19	18	T4	200	490	3	12	67	190	0	1	2

MASTER CHART

S. No	t-T10	t-sensory	t-motor	max sensory	t-2 segment regression	Duration of analgesia	Sedation score	Ephedrine used	Lowest MAP	Duration of surgery	Intra op EPIDURAL top up	post op rescue	Patient acceptance score
GROUP - C													
1.	19	19	32	T10	140	240	0	6	64	180	1	3	2
2.	18	18	30	T10	120	300	1	0	72	190	2	4	1
3.	20	20	28	T10	120	280	1	6	65	240	2	3	1
4.	19	19	32	T10	100	320	0	6	68	180	1	4	1
5.	19	19	30	T10	140	280	0	6	68	180	1	4	0
6.	17	17	25	T10	150	300	0	12	62	180	1	3	0
7.	18	20	28	T8	100	420	0	6	69	150	0	2	0
8.	19	19	32	T10	110	280	1	6	64	180	0	3	2
9.	20	20	29	T10	120	240	0	0	70	180	1	3	2
10.	21	21	34	T10	140	300	0	0	82	200	1	3	1
11.	16	16	26	T10	100	360	0	6	68	180	1	3	1
12.	20	24	32	T8	100	300	1	6	66	190	1	3	1
13.	18	18	25	T10	90	210	1	0	74	150	0	3	1
14.	21	21	32	T10	120	240	1	0	80	180	1	3	2
15.	20	20	31	T10	140	270	0	6	66	180	0	2	1
16.	18	18	26	T10	150	210	0	12	64	200	2	3	1
17.	18	18	28	T10	110	280	0	6	68	180	1	2	1
18.	17	17	26	T10	120	320	0	0	76	120	0	3	1
19.	19	19	30	T10	100	300	0	0	72	170	1	2	0
20.	17	20	30	T8	100	270	1	0	74	160	0	2	0

MASTER CHART

S.No	Base Line	**15 min**	**30 min**	**60 min**	**90 min**	**120 min**	**150 min**	**180 min**	**240 min**	**6 hrs**	**8 hrs**	**10 hrs**	**12 hrs**	**16 hrs**	**20 hrs**	**24 hrs**
PULSE RATE – GROUP A																
1.	81	58	56	56	57	58	59	59	58	58	56	59	57	58	60	67
2.	91	59	61	60	60	61	62	62	59	63	61	61	62	60	60	76
3.	84	65	64	67	66	65	68	65	69	65	65	66	66	67	64	66
4.	88	58	56	57	57	55	59	57	58	57	56	57	58	58	59	78
5.	88	64	64	63	63	62	61	66	63	60	62	63	61	60	63	74
6.	84	55	58	58	47	49	54	55	49	57	56	52	55	55	54	70
7.	77	66	66	65	67	67	64	64	63	63	63	63	63	64	62	78
8.	78	66	66	65	67	66	63	66	67	66	65	66	65	67	68	66
9.	79	59	58	57	60	58	57	58	57	59	57	56	58	57	58	64
10.	90	58	58	59	60	59	59	58	57	59	59	59	58	59	59	65
11.	94	67	66	69	70	71	73	69	68	68	69	69	69	68	67	78
12.	88	66	66	67	68	68	67	67	66	68	66	66	67	67	66	85
13.	81	77	76	76	75	74	76	79	71	69	72	71	77	76	75	80
14.	84	70	70	71	71	71	72	71	70	71	70	72	73	71	71	74
15.	81	67	66	68	69	68	68	69	70	69	69	68	69	69	65	69
16.	87	54	55	49	49	54	52	52	53	54	55	49	48	55	53	68
17.	90	58	60	59	59	58	58	57	59	59	58	57	58	58	56	64
18.	79	57	60	59	58	59	56	57	59	58	59	58	58	58	58	62
19.	76	59	59	60	58	59	59	57	60	63	59	58	59	60	59	78
20.	82	67	63	63	60	60	59	62	61	58	62	60	60	61	61	76
21.	86	66	63	62	61	60	58	60	62	60	64	62	58	61	60	76
22.	87	59	59	58	58	60	61	61	62	62	59	60	61	62	60	66
23.	90	68	69	66	67	69	66	67	66	69	66	65	70	68	62	68
24.	96	67	66	66	65	65	65	66	59	64	64	64	62	60	61	78
25.	93	57	59	59	60	60	60	61	60	61	61	58	58	56	59	72
26.	98	59	58	57	60	58	57	58	57	59	57	56	58	57	58	64
27.	84	58	58	59	60	59	59	58	57	59	59	59	58	59	59	65
28.	89	67	66	69	70	71	73	69	68	68	69	69	69	68	67	78
29.	90	66	66	67	68	68	67	67	66	68	66	66	67	67	66	85
30.	88	77	76	76	75	74	76	79	71	69	72	71	77	76	75	80

MASTER CHART

S.No	Base Line	**15 min**	**30 min**	**60 min**	**90 min**	**120 min**	**150 min**	**180 min**	**240 min**	**6 hrs**	**8 hrs**	**10 hrs**	**12 hrs**	**16 hrs**	**20 hrs**	**24 hrs**
PULSE RATE – GROUP B																
1.	81	100	78	70	69	77	72	73	74	77	83	84	83	83	81	84
2.	102	91	87	79	80	81	82	83	83	90	98	89	85	81	86	82
3.	99	84	78	76	73	75	78	82	81	88	89	83	82	72	77	78
4.	97	88	83	76	80	80	80	78	72	77	79	79	79	76	72	73
5.	94	88	78	78	85	77	72	72	69	71	71	75	80	81	74	79
6.	91	84	76	74	75	75	74	70	73	75	78	78	76	75	73	76
7.	85	77	72	79	76	77	75	76	82	84	92	92	81	79	88	81
8.	82	78	72	76	77	72	71	76	79	87	83	82	84	79	78	72
9.	85	79	79	71	71	70	78	72	78	84	92	85	83	78	81	81
10.	82	90	77	83	79	79	79	74	84	85	84	85	83	82	86	83
11.	96	94	79	82	75	72	76	76	76	79	79	77	74	79	81	86
12.	92	88	83	79	80	81	74	84	86	90	90	91	57	85	88	84
13.	105	81	75	71	78	76	75	78	76	75	79	82	80	80	79	78
14.	92	84	77	76	71	77	74	77	78	88	90	89	78	82	80	81
15.	91	81	77	75	74	74	75	75	78	85	86	84	81	80	80	84
16.	96	87	71	71	70	73	78	84	80	79	82	81	80	78	78	77
17.	94	90	77	70	74	74	77	80	80	82	88	91	84	84	82	85
18.	89	79	81	75	77	76	73	70	69	76	83	82	72	74	75	80
19.	96	76	85	76	71	72	72	82	77	73	76	79	85	77	79	80
20.	88	82	76	67	75	74	70	75	74	71	71	67	76	78	73	74
21.	87	86	85	84	79	74	71	69	69	74	74	65	78	79	74	87
22.	92	87	86	79	76	77	70	75	83	91	91	89	81	81	82	86
23.	103	90	76	74	71	77	78	82	82	97	95	92	81	82	78	88
24.	111	96	80	76	75	75	75	77	76	77	79	92	79	77	77	76
25.	99	93	85	78	74	78	75	78	84	81	81	83	80	76	79	83
26.	78	92	85	76	76	72	74	65	60	55	52	60	62	74	69	66
27.	82	84	83	78	79	82	78	74	74	75	78	79	80	86	66	68
28.	82	88	83	87	84	64	66	81	86	83	84	82	76	87	80	87
29.	80	82	85	95	86	67	79	62	65	67	60	56	52	106	87	81
30.	80	92	87	109	87	69	85	71	72	75	74	71	78	110	102	76

MASTER CHART

S.No	Base Line	**15 min**	**30 min**	**60 min**	**90 min**	**120 min**	**150 min**	**180 min**	**240 min**	**6 hrs**	**8 hrs**	**10 hrs**	**12 hrs**	**16 hrs**	**20 hrs**	**24 hrs**
PULSE RATE – GROUP C																
1.	82	93	91	79	70	71	87	66	64	68	60	56	84	86	80	86
2.	82	102	91	108	66	74	75	71	76	75	74	72	80	66	69	69
3.	77	87	86	79	64	74	70	74	75	81	82	85	84	64	62	60
4.	82	84	82	85	68	65	68	64	68	60	56	84	89	71	76	75
5.	84	97	93	86	69	69	69	75	68	69	64	68	71	74	75	81
6.	81	93	88	103	77	70	63	74	75	81	82	85	84	64	68	60
7.	85	85	86	92	90	81	62	64	68	60	56	84	89	75	68	69
8.	78	96	80	90	73	74	64	75	68	69	64	68	71	72	75	71
9.	82	92	93	101	69	66	67	84	86	74	76	67	75	70	79	78
10.	73	86	83	86	66	68	65	85	80	76	84	72	78	65	60	55
11.	76	84	77	87	80	87	64	84	86	88	89	80	88	74	74	75
12.	82	101	85	106	87	81	62	69	69	60	68	62	79	81	86	83
13.	73	100	82	110	102	76	75	62	60	70	74	72	74	62	65	67
14.	78	90	74	89	88	90	85	70	64	75	70	74	71	71	72	75
15.	78	76	86	86	80	86	84	70	71	87	66	64	84	70	74	75
16.	79	80	88	85	87	78	68	66	74	75	71	76	89	66	64	68
17.	81	89	90	87	85	77	71	64	74	70	74	75	71	71	76	75
18.	84	93	88	74	75	81	82	85	65	68	64	68	95	60	68	62
19.	75	90	78	64	68	60	56	84	69	69	75	68	67	70	74	72
20.	81	89	79	90	73	74	64	75	68	69	64	68	71	72	75	71